(FILE 'HCAPLUS' ENTERED AT 12:36:16 ON 13 DEC 2002)

L1 15825 SEA FILE=HCAPLUS ABB=ON PLU=ON CTL OR CYTOTOX?(W)T(W)(LYMPHOCYT? OR CELL)

L2 4228 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND (INFECTIO## OR HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W)SYNDROM?)

L3 1326 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (TREAT? OR THERAP? OR IMMUNOGEN?)

L4 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND (HYBRIDIS? OR HYBRIDIZ? OR MICROARRAY? OR MICRO ARRAY?)

L1 15825 SEA FILE=HCAPLUS ABB=ON PLU=ON CTL OR CYTOTOX?(W)T(W)(LYMPHOCYT? OR CELL)

L2 4228 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND (INFECTIO## OR HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W)SYNDROM?)

L5 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (HYBRIDIS? OR HYBRIDIZ? OR MICROARRAY? OR MICRO ARRAY?)

L6 24 S L4 OR L5

L6 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:658581 HCAPLUS
DOCUMENT NUMBER: 137:215802
TITLE: Computerized method for optimizing minigenes and designing multi-epitope vaccines
INVENTOR(S): Sette, Alessandro; Chesnut, Robert; Livingston, Brian D.; Baker, Denise Marie; Newman, Mark J.; Brown, David H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of Appl. PCT/US00/35568.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002119127	A1	20020829	US 2001-894018	20010627
WO 2001047541	A1	20010705	WO 2000-US35568	20001228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2002083714	A2	20021024	WO 2002-US9877	20020328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-173390P P 19991228
WO 2000-US35568 A2 20001228
US 2001-284221P P 20010416
US 2001-894018 A 20010627

AB The invention relates to the field of biol. In particular, the invention relates to a method and system for designing optimized multi-epitope vaccines having selected combinations of amino acid insertions at the junctions of the multi-epitope constructs so as to minimize the no. of junctional epitopes and provide vaccines with increased **immunogenicity**. Multi-epitope constructs comprising two or more **cytotoxic T lymphocyte** epitope nucleic acids and encoded protein, e.g. EP-**HIV**-1090, **HIV**-CPT, **HIV**-FT, **HIV**-TC, HCV.1, HCV.2, HCV.3s1, HCV.3s2, HCV.3s2(-3), HCV.3s3, HCV.PC3, HCV.PC4, HCV.2431(1P), HCV.4312(1P), AOSI.K, HBV.1, HBV.2, PfCTL.1, PfCTL.2, PfCTL.3, Pf33, TB.1, BCL A2#90, BCL A2#88, BCL A2#63, Prostate 1, **HIV**-1043, **HIV**-1043 PADRE, HIV75mer, and PfHTL were prepd. for the purpose of the invention.

L6 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:595035 HCAPLUS
DOCUMENT NUMBER: 137:168254
TITLE: Superior molecular vaccine based on self-replicating RNA, suicidal DNA or naked DNA vector, that links antigen with polypeptide that promotes antigen presentation for **treating** cancer and **infections**
INVENTOR(S): Wu, Tzyy-Choou; Hung, Chien-Fu
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061113	A2	20020808	WO 2002-US2598	20020201

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,

CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-265334P P 20010201

AB Improved mol. vaccines comprise nucleic acid vectors that encode a fusion polypeptide that includes polypeptide or peptide phys. linked to an antigen. The linked polypeptide is one that (a) promotes processing of the expressed fusion polypeptide via the MHC class I pathway and/or (b) promotes development or activity of antigen presenting cells, primarily dendritic cells. These vaccines employ one of several types of nucleic acid vectors, each with its own relative advantages: naked DNA plasmids, self-replicating RNA replicons and suicidal DNA-based on viral RNA replicons. Administration of such a vaccine results in enhance immune responses, primarily those mediated by CD8+ **cytotoxic T lymphocytes**, directed against the immunizing antigen part of the fusion polypeptide. Such vaccines are useful against tumor antigens, viral antigens and antigens of other pathogenic microorganisms and can be used in the prevention or **treatment** of diseases that include cancer and **infections**.

L6 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123514 HCAPLUS
DOCUMENT NUMBER: 136:182454
TITLE: Methods for identifying and producing antigens for **treating** cancer and **infection**
INVENTOR(S): Zauderer, Maurice
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp., Division of U.S. Ser. No. 935,377.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002018785	A1	20020214	US 2001-822250	20010402

PRIORITY APPLN. INFO.: US 1997-935377 A3 19970922

AB The present invention relates to novel methods for the identification of antigens recognized by **cytotoxic T cells** (**CTLs**) and specific for human tumors, cancers, and infected cells, and the use of such antigens in **immunogenic** compns. or vaccines to induce regression of tumors, cancers, or **infections** in mammals, including humans. The invention encompasses methods for induction and isolation of **cytotoxic T cells** specific for human tumors, cancers and infected cells, and for improved selection of genes that encode the target antigens recognized by these specific T cells. The invention also relates to differential display methods that improve resoln. of, and that reduce the frequency of false positives of DNA fragments that are differentially expressed in tumorous, cancerous, or infected tissues vs. normal tissues. The invention further relates to the engineering of recombinant viruses as expression vectors for tumor,

cancer, or infected cell-specific antigens.

L6 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:107056 HCAPLUS
DOCUMENT NUMBER: 136:166049
TITLE: Molecular vaccine linking intercellular spreading protein to an antigen
INVENTOR(S): Wu, Tzyy-Choou; Hung, Chien-Fu
PATENT ASSIGNEE(S): The John Hopkins University, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009645	A2	20020207	WO 2001-US23966	20010801
WO 2002009645	A3	20021017		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001090520	A5	20020213	AU 2001-90520		20010801
PRIORITY APPLN. INFO.:			US 2000-222185P	P	20000801
			US 2001-268575P	P	20010215
			US 2001-281004P	P	20010404
			WO 2001-US23966	W	20010801

AB Superior mol. vaccines comprise nucleic acids, including naked DNA and replicon RNA, that encode a fusion polypeptide that includes an antigenic peptide or polypeptide against which an immune response is desired. Fused to the antigenic peptide is an intercellular spreading protein, in particular a herpes virus protein VP22 or a homolog or functional deriv. thereof. Preferred spreading proteins are VP22 from HSV-1 and Marek's disease virus. The nucleic acid can encode any antigenic epitope of interest, preferably an epitope that is processed and presented by MHC class I proteins. Antigens of pathogenic organisms and cells such as tumor cells are preferred. Vaccines comprising HPV-16 E7 oncoprotein are exemplified. Also disclosed are methods of using the vaccines to induce heightened T cell mediated immunity, in particular by **cytotoxic T lymphocytes**, leading to protection from or **treatment** of a tumor.

L6 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:364686 HCAPLUS
DOCUMENT NUMBER: 135:2592
TITLE: Transcriptional regulation of the urease operon in Helicobacter pylori in response to pH and mechanisms of stable colonization in the stomach

AUTHOR(S): Shirai, Mutsunori
CORPORATE SOURCE: Dep. Microbiol. Reprod., Pediatr. Infect. Sci., Yamaguchi Univ. Sch. Med., Ube, Yamaguchi, 755-8505, Japan
SOURCE: Yamaguchi Igaku (2001), 50(2), 593-601
CODEN: YIKUAO; ISSN: 0513-1731
PUBLISHER: Yamaguchi Daigaku Igakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 26 refs. Helicobacter pylori is known to colonize in the human stomach by neutralizing acidic condition with urease activity. The effect of acid on the transcription of the urease operon was investigated to det. whether H. pylori is has a novel mechanism under such conditions. We investigated the transcription of the urease gene cluster ureABIEFGH in Helicobacter pylori to det. the regulation of gene expression of the highly produced enzyme urease. Northern blot **hybridization** anal. demonstrated that cells of the wild-type strain grown in an ordinary broth had transcripts of ureAB, ureABI, ureI, ureIE' and ure'FGH, but cells of a ureI-disrupted mutant had only the ureAB transcript. When the wild-type cells were exposed to pH 8 for 30 min, very little mRNA was detected. However, when exposed to pH 6, a large amt. of the ureIE" transcript, which was longer than the ureIE' transcript, together with the addnl. transcripts ureABIEFGH and ure'EFGH were detected. Rifampicin addn. expts. demonstrated that urease mRNAs, and the ureIE' transcripts in particular, are more stable at pH 5.5 than at pH 7. In accord with these results, urease activity in the crude cell ext. of the pH 5.5 culture was twice as much as that of the pH 7 culture, although the amts. of UreA and UreB detected by immunoblot anal. were similar. The transcription start point of ureI was identified by primer extension using a ureA promoter-deleted mutant, and a consensus sequence of RpoD-RNA polymerase was found in the ureI promoter. The 3' end of the ureIE" mRNA, detd. using S1 nuclease mapping, revealed that the transcript is able to cover the majority of the ureE open reading frame (ORF) that might be sufficient for UreE activity. Based on the above results, we conclude that the urease gene cluster of H. pylori consists of two operons, ureAB and ureIEFGH, and that primary transcripts of the latter as well as the read-through transcript, ureABIEFGH, are cleaved to produce several species of mRNA. It has been suggested that the ureIEFGH operon is regulated post-transcriptionally by mRNA decay in response to environmental pH. We are tempted to speculate that the ureE" transcript present in acidic pH may contribute to produce an active product that can proceed the nickel incorporation to the active center, the final step of urease biosynthesis. On the other hand, Th1 and Th2 cells play a central role in immunoregulation during **infection**. We show that H. pylori induces Th1 cytokine responses early (2 wk) but predominantly Th2 responses later (6 wk) in **infection**. The switch is principally mediated by urease-specific CD4(+) T cells, and correlates with a loss of urease-specific high-avidity JNK(+) Th1 and gain of low-avidity JNK(-) (possibly Th2) cells at the later stage of **infection**, concomitant wit ha 100-fold higher colonization level of H. pylori at 6 wk than at 2 wk that might tolerize high-avidity Th1 cells. Furthermore, differentiation of **HIV** gp160-specific CD4(+) Th and CD8(+) **cytotoxic T lymphocytes** (**CTL**) into effector cells is impaired in 6-wk H. pylori-infected mice

immunized with vaccinia expressing gp160, and serum IL-12 stimulated by vaccinia **infection** is barely detectable. Adoptive transfer of urease-specific Th2 cells to mice infected only with gp160-expressing vaccinia abrogates Th1 polarization of the gp120 response, down-modulates virus-specific **CTL** responses, and delays virus clearance. Therefore, the H. pylori urease-mediated immunoregulation in the switch from JNK(+) Th1 to JNK(-) Th2 phenotype, and the preceding low IL-12 response, are likely crit. steps in the impairment of antiviral immunity. Other some novel mechanisms of H. pylori colonization and the strain diversity which we obtained were described and discussed in the text.

L6 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:785188 HCAPLUS
DOCUMENT NUMBER: 132:133037
TITLE: Molecular characterization of the guinea pig cytomegalovirus UL83 (pp65) protein homolog
AUTHOR(S): Schleiss, Mark R.; Mcgregor, Alistair; Jensen, Nancy J.; Erdem, Guliz; Aktan, Laurie
CORPORATE SOURCE: Division of Infectious Diseases, Children's Hospital Research Foundation, Cincinnati, OH, 45229, USA
SOURCE: Virus Genes (1999), 19(3), 205-221
CODEN: VIGEET; ISSN: 0920-8569
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tegument phosphoproteins of human cytomegalovirus (HCMV) elicit **cytotoxic T-lymphocyte** (**CTL**) responses and are hence candidates for subunit vaccine development. Little is known, however, about the tegument proteins of nonhuman cytomegaloviruses, such as guinea pig CMV (GPCMV). DNA sequence anal. of the Eco R I "C" fragment of the GPCMV genome identified an open reading frame (ORF) which is colinear with that of the HCMV tegument phosphoprotein, UL83 (pp65). This ORF was found to have identity to HCMV UL83 and was predicted to encode a 565-amino-acid (aa) protein with a mol. mass of 62.3 kDa. Transcriptional analyses revealed that a GPCMV UL83 probe **hybridized** with both 2.2kb and 4.2kb mRNA species at 48 h post-**infection** (p.i.); synthesis of these messages was blocked by phosphonoacetic acid (PAA), defining these as "late" gene transcripts. In vitro translation of the UL83 ORF in reticulocyte lysate resulted in synthesis of a 65 kDa protein. Immunofluorescence expts. revealed that the putative GPCMV UL83 homolog exhibited a predominantly nuclear localization pattern. Polyclonal antisera were raised against a UL83/glutathione-S-transferase (GST) fusion protein. This antibody identified a 70-kDa virion-assocd. protein, the putative GPCMV UL83 homolog, in immunoblot and radioimmunopptn. expts. Labeling expts. with 32P-orthophosphate indicated that the GPCMV UL83 protein is phosphorylated. Western blot anal. of glycerol tartrate gradient-purified virions and dense bodies confirmed that the putative GPCMV UL83 homolog was a constituent of both fractions.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:745332 HCAPLUS

DOCUMENT NUMBER: 130:94379
TITLE: Inactivating mutations in an SH2 domain-encoding gene in X-linked lymphoproliferative syndrome
AUTHOR(S): Nichols, Kim E.; Harkin, D. Paul; Levitz, Seth; Krainer, Michael; Kolquist, Kathryn Ann; Genovese, Cameo; Bernard, Amy; Ferguson, Martin; Zuo, Lin; Snyder, Eric; Buckler, Alan J.; Wise, Carol; Ashley, Jennifer; Lovett, Michael; Valentine, Marcus B.; Look, A. Thomas; Gerald, William; Housman, David E.; Haber, Daniel A.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(23), 13765-13770
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB X-linked lymphoproliferative syndrome (XLP) is an inherited immunodeficiency characterized by increased susceptibility to Epstein-Barr virus (EBV). In affected males, primary EBV **infection** leads to the uncontrolled proliferation of virus-contg. B cells and reactive **cytotoxic T cells**, often culminating in the development of high-grade lymphoma. The XLP gene has been mapped to chromosome band Xq25 through linkage anal. and the discovery of patients harboring large constitutional genomic deletions. The authors describe here the presence of small deletions and intragenic mutations that specifically disrupt a gene named DSHP in 6 of 10 unrelated patients with XLP. Ths gene encodes a predicted protein of 128 amino acids composing a single SH2 domain with extensive homol. to the SH2 domain of SHIP, an inositol polyphosphate 5-phosphatase that functions as a neg. regulator of lymphocyte activation. DSHP is expressed in transformed T cell lines and is induced following in vitro activation of peripheral blood T lymphocytes. Expression of DSHP is restricted in vivo to lymphoid tissues, and RNA in situ **hybridization** demonstrates DSHP expression in activated T and B cell regions of reactive lymph nodes and in both T and B cell neoplasms. These observations confirm the identity of DSHP as the gene responsible for XLP, and suggest a role in the regulation of lymphocyte activation and proliferation. Induction of DSHP may sustain the immune response by interfering with SHIP-mediated inhibition of lymphocyte activation, while its inactivation in XLP patients results in a selective immunodeficiency to EBV.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:463998 HCAPLUS
DOCUMENT NUMBER: 129:188277
TITLE: Intestinal intraepithelial lymphocytes are primed for gamma interferon and MIP-1.beta. expression and display antiviral cytotoxic activity despite severe CD4+ T-cell depletion in primary simian immunodeficiency virus

infection

AUTHOR(S): Mattapallil, Joseph J.; Smit-Mcbride, Zeljka; Mcchesney, Michael; Dandekar, Satya

CORPORATE SOURCE: Department of Internal Medicine, Division of Infectious Diseases, School of Medicine, University of California, Davis, CA, 95616, USA

SOURCE: Journal of Virology (1998), 72(8), 6421-6429
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Intraepithelial lymphocytes (IEL) are a crit. effector component of the gut-assocd. lymphoid tissue (GALT) and play an important role in mucosal immunity as well as in the maintenance of the epithelial cell integrity and barrier function. The objective of this study was to det. whether simian immunodeficiency virus (SIV) **infection** of rhesus macaques would cause alterations in the immunophenotypic profiles of IEL and their mitogen-specific cytokine (gamma interferon [IFN-.gamma.] and MIP-1.beta.) responses (by flow cytometry) and virus-specific **cytotoxic T-cell** (**CTL**) activity (by the chromium release assay). Virally infected IEL were detected through the entire course of SIV **infection** by in situ **hybridization**. Severe depletion of CD4+ single-pos. and CD4+CD8+ double-pos. T cells occurred early in primary SIV **infection**, which was coincident with an increased prevalence of CD8+ T cells. This was in contrast to a gradual depletion of CD4+ T cells in peripheral blood. The CD8+ IEL were the primary producers of IFN-.gamma. and MIP-1.beta. and were found to retain their potential to produce both IFN-.gamma. and MIP-1.beta. through the entire course of SIV **infection**. SIV-specific **CTL** activity was detected in primary IEL at 1, 2, and 4 wk post-SIV **infection**. These results demonstrated that IEL may be involved in generating antiviral immune responses early in SIV **infection** and in suppressing viral **infection** thereafter. Alterations in homeostasis in epithelia due to severe CD4+ T-cell depletion accompanied by changes in the cytokine and chemokine prodn. by IEL may play a role in the enteropathogenesis of SIV **infection**.

L6 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:368321 HCAPLUS

DOCUMENT NUMBER: 129:147947

TITLE: Characterization of the cutaneous exanthem in macaques infected with a Nef gene variant of SIVmac239

AUTHOR(S): Sasseville, Vito G.; Rottman, James B.; Du, Zhenjian; Veazey, Ronald; Knight, Heather L.; Caunt, Diane; Desrosiers, Ronald C.; Lackner, Andrew A.

CORPORATE SOURCE: Division of Comparative Pathology New England Regional Primate Research Center, Harvard Medical School, Southborough, MA, 01772-9102, USA

SOURCE: Journal of Investigative Dermatology (1998), 110(6), 894-901
CODEN: JIDEAE; ISSN: 0022-202X

PUBLISHER: Blackwell Science, Inc.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The molecularly cloned viruses known as SIVmac239/R17Y and SIVmac239/YEnef cause extensive lymphocyte activation and induce an acute disease syndrome in macaque monkeys. One manifestation of this syndrome is a severe diffuse cutaneous maculopapular exanthem that is similar to the exanthem assocd. with **HIV-1 infection**. To examine the pathogenesis of this exanthem, biopsies obtained throughout the course of clin. evident rash were examd. for the presence of virus by in situ **hybridization** and immunohistochem., and the cellular infiltrate was characterized with respect to cellular immunophenotype and chemokine receptor expression. The onset of rash was assocd. with abundant simian immunodeficiency virus nucleic acid and protein within perivascular dermal infiltrates and occasionally within intraepithelial cells. Anal. of cellular infiltrates showed that biopsies, obtained on the day of rash onset, were composed of equal nos. of CD4+ and CD8+ lymphocytes and abundant .alpha.E.beta.7 pos. cells surrounding vessels with upregulated endothelial E-selectin. Moreover, by examg. virus expression in sequential skin biopsies from the same animal, the clearance of virus and the resoln. of rash were assocd. with an increase in the percentage of cells expressing CD8, the chemokine receptor CXCR3, and GMP-17, a marker of cytotoxic granules. These results suggest that activated **cytotoxic T cells** are trafficking to sites of inflammation in the skin and directly or indirectly affect levels of viral replication at these sites.

L6 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:266330 HCAPLUS
DOCUMENT NUMBER: 129:26910
TITLE: Virus-specific CD4+ T cells eliminate Borna disease virus from the brain via induction of cytotoxic CD8+ T cells
AUTHOR(S): Noske, Kerstin; Bilzer, Thomas; Planz, Oliver; Stitz, Lothar
CORPORATE SOURCE: Institut fur Virologie, Justus-Liebig-Universitat Giessen, Germany
SOURCE: Journal of Virology (1998), 72(5), 4387-4395
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Persistent Borna disease virus **infection** of the brain can be prevented by **treatment** of naive rats with a virus-specific CD4+ T-cell line prior to **infection**. In rats receiving this **treatment**, only a transient low-level encephalitis was seen compared to an increasingly inflammatory reaction in untreated infected control rats. Virus replication was found in the brain for several days after **infection** before the virus was cleared from the central nervous system. The loss of infectivity from the brain was confirmed by neg. results by reverse transcription-PCR with primers for mRNA, by in situ **hybridization** for both genomic and mRNA, and by immunohistol. Most importantly, in vitro assays revealed that the T-cell line used for transfusion had no cytotoxic capacity. The kinetics of virus clearance were paralleled by the appearance of CD8+ T cells and the expression of perforin in the brain. Testing

of lymphocytes isolated from the brains of CD4+ T-cell-**treated** rats after challenge revealed high cytotoxic activity due to the presence of CD8+ **cytotoxic T cells** at time points when brain lymphocytes from infected control rats induced low-level cytolysis of target cells. Neutralizing antiviral antibodies and gamma interferon were shown not to be involved in the elimination of virus from the brain.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:267348 HCAPLUS
DOCUMENT NUMBER: 124:314615
TITLE: Major histocompatibility complex class I expression on neurons in subacute sclerosing panencephalitis and experimental subacute measles encephalitis
AUTHOR(S): Gogate, Nitin; Swoveland, Peggy; Yamabe, Toshio; Verma, Lalit; Woyciechowska, Joanna; Tarnowska-Dziduszko, Eugenia; Dymecki, Jerzy; Dhib-Jalbut, Suhayl
CORPORATE SOURCE: Department of Neurology, University of Maryland Hospital, Baltimore, MD, 21201, USA
SOURCE: Journal of Neuropathology and Experimental Neurology (1996), 55(4), 435-43
CODEN: JNENAD; ISSN: 0022-3069
PUBLISHER: American Association of Neuropathologists, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lack of major histocompatibility class I antigens on neurons has been implicated as a possible mechanism for viral persistence in the brain since these antigens are required for **cytotoxic T-lymphocyte** recognition of infected cells. In subacute sclerosing panencephalitis (SSPE), measles virus (MV) persists in neurons, resulting in a fatal chronic **infection**. MHC class I mRNA expression was examd. in formalin-fixed brain tissue from 6 SSPE patients by in situ **hybridization.** In addn. MHC class I protein expression in MV-infected neurons was examd. in exptl. subacute measles encephalitis (SME) by double immunohistochem. MHC class I mRNA expression was upregulated in SSPE tissues studied, and in 5 out of 6 cases the expression was definitively seen on neurons. The percentage of neurons expressing MHC class I mRNA ranged between 20-84% in infected areas. There was no correlation between the degree of **infection** and expression of MHC class I mols. on neurons. Importantly, the no. of neurons co-expressing MHC class I and MV antigens was markedly low, varying between 2-8%. Similar results were obtained in SME where 20-30% of the neurons expressed MHC class I but <8% co-expressed MHC class I and MV antigens. Perivascular infiltrating cells in the infected regions in SME expressed IFN.gamma. immunoreactivity. Thus, MV may not be directly involved in the induction of MHC class I on neurons and cytokines such as IFN.gamma. may play an important role. Furthermore, the paucity of neurons co-expressing MHC class I and MV antigens in SSPE and SME suggests that such cells are either rapidly cleared by **cytotoxic T lymphocytes** (**CTL**), or, alternatively, lack of co-expression of MHC class I on MV infected neurons favors MV

persistence in these cells by escaping **CTL** recognition.

L6 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:147170 HCAPLUS
DOCUMENT NUMBER: 124:229727
TITLE: A model of latent adenovirus 5 **infection** in the guinea pig (Cavia porcellus)
AUTHOR(S): Vitalis, Timothy Z.; Keicho, Naoto; Itabashi, Shigeru; Hayashbi, Shizu; Hogg, James C.
CORPORATE SOURCE: St. Paul's Hosp., Univ. British Columbia Pulmonary Res. Lab., Vancouver, BC, Can.
SOURCE: American Journal of Respiratory Cell and Molecular Biology (1996), 14(3), 225-31
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Lung Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A model of adenovirus 5 (Ad5) **infection** was developed in guinea pigs to begin to study its role in the pathogenesis of peripheral lung inflammation. Forty animals were inoculated intranasally with 107.0 pfu of Ad5/animal, and 15 animals inoculated with sterile culture media served as controls. Viral titers were 104.4, 106.1, 105.2, and 102.9 pfu/animal, on days 1, 3, 4, and 7 after **infection**, resp. In situ **hybridization** to viral DNA and immunocytochem. for Ad5 E1A protein localized the virus to airway and alveolar epithelial cells. Histol. examn. showed an extensive inflammatory cell infiltration around the airways, with epithelial necrosis and an alveolar exudate that caused localized alveolar collapse in the infected areas. Immunocytochem. identified the cells in the infiltrate as **cytotoxic T cells**. Although all animals 20 and 47 days after **infection** had seroconverted to Ad5, virus was not detected in these groups either by viral plaque assay or in situ **hybridization**. Ad5 E1A DNA was detected by polymerase chain reaction in five of six animals 20 days after **infection** and in five of five animals 47 days after **infection**. In these same animals, E1A protein was detected 20 days after **infection** in two and 47 days after **infection** in one while persistent bronchiolitis was obsd. in four and three animals 20 and 47 days after **infection**, resp. These results demonstrate that the guinea pig provides a useful model to study the role of Ad5 **infection** in chronic airway inflammation.

L6 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:381668 HCAPLUS
DOCUMENT NUMBER: 122:158460
TITLE: Mechanism of interleukin 12-mediated toxicities during experimental viral **infections**: role of tumor necrosis factor and glucocorticoids
AUTHOR(S): Orange, Jordan S.; Salazar-Mather, Thais P.; Opal, Steven M.; Spencer, Robert L.; Miller, Andrew H.; McEwen, Bruce S.; Biron, Christine A.
CORPORATE SOURCE: Division of Biology and Medicine, Brown Univ., Providence, RI, 02912, USA
SOURCE: Journal of Experimental Medicine (1995), 181(3), 901-14

CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interleukin 12 (IL-12) doses in excess of 100 ng/day have been shown to induce profound immunotoxicities in mice infected with lymphocytic choriomeningitis virus (LCMV). These immunotoxicities are characterized by almost complete inhibition of virus-induced CD8+ T cell expansion and **CTL** activation, and up to 2 log increases in viral replication. They are accompanied by induction of serum tumor necrosis factor (TNF). The studies here were undertaken to characterize mechanisms for the IL-12-induced toxicities and to examine expression and function of TNF in this context. Several physiol. changes were induced in IL-12-**treated** uninfected and dramatically elevated in IL-12-**treated** virus-infected mice. IL-12 induced (a) decreases in body wts., >10% in uninfected and >20% in LCMV-infected mice; (b) elevation of circulating glucocorticoid levels to >10 .mu.g/dL in uninfected and >20 .mu.g/dL in infected mice; and (c) decreases in thymic mass, >30% in uninfected and up to 95% in infected mice. These changes are known to be assocd. with circulating TNF. Northern blot and in situ **hybridization** analyses demonstrated that IL-12 induced TNF-.alpha. expression and that LCMV **infection** synergized with IL-12 for induction of this factor. Antibodies neutralizing TNF reversed all of the IL-12-induced toxicities in LCMV-infected mice including the immunotoxicities against CD8+ T cells and anti-viral defenses. The TNF-mediated immunotoxicities appeared to result from an induced cellular sensitivity to the factor, as splenic leukocytes and CD8+ T cell subsets isolated from LCMV-infected mice were more sensitive to TNF-mediated cytotoxicity in culture than were equiv. populations prepd. from uninfected mice. Expts. with the glucocorticoid type II receptor antagonist, RU486, demonstrated that endogenous glucocorticoids were secondary intermediaries in IL-12-induced thymic atrophy. Studies in IL-2-deficient mice showed that the synergism was dependent upon endogenous IL-2. The results delineate a unique mechanism of TNF-mediated toxicity. They also have implications concerning potential detrimental consequences of in vivo TNF induction and of IL-12 administration for protective anti-viral responses.

L6 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:223910 HCAPLUS
DOCUMENT NUMBER: 122:7884
TITLE: Induction by concanavalin A of specific mRNAs and cytolytic function in a CD8-positive T cell hybridoma
AUTHOR(S): Gu, Jing Jin; Harriss, June V.; Ozato, Keiko; Gottlieb, Paul D.
CORPORATE SOURCE: Dep. Microbiol., Univ. Texas, Austin, TX, 78712, USA
SOURCE: Journal of Immunology (1994), 153(10), 4408-17
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A previous report from this lab. described the prodn. of CD8+, class-specific T cell hybridomas which developed specific cytolytic

activity and the ability to secrete IL-2 upon Con A or specific Ag stimulation. Unlike normal lymphocytes or long-term **CTL** lines for which exposure to Ag triggers both differentiation and proliferation, T cell hybridoma lines can be activated functionally against a background of continuous proliferation. They therefore provide a unique system with which to study the mol. events involved in the induction of cytolytic function. The expression of mRNA from a series of genes was evaluated by Northern **hybridization** at various times after Con A stimulation of the H-2Ld-specific CD8+ 3D9 hybridoma. Induction of the c-fos proto-oncogene by 45 min poststimulation was followed shortly by c-myc induction. Perforin mRNA was expressed at a low level in the unstimulated hybridomas, but was down-regulated upon Con A stimulation to levels undetectable by PCR. Interestingly, prodn. of granzyme A mRNA was strongly induced by 45 min after Con A stimulation. In the CD8+ RT-1.3G3 hybridoma, which is nonlytic and specific for the **HIV**-1 envelope glycoprotein, c-fos but not granzyme A mRNA was induced by 45 min poststimulation, and no granzyme A mRNA was detectable at any time. Thus, a significant role for granzyme A in the induction of cytolytic activity is suggested. Cytolysis by the 3D9 hybridoma involved both target cell membrane damage and DNA fragmentation, and both Ca2+-dependent and Ca2+-independent cytolysis were obsd. Although TNF-.alpha. mRNA was induced by 4 h poststimulation, Ab to TNF-.alpha. failed to inhibit the Ca2+-independent lysis obsd., leaving the basis for the obsd. Ca2+-independent lysis unexplained.

L6 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:602064 HCAPLUS
DOCUMENT NUMBER: 121:202064
TITLE: Gastric carcinoma: monoclonal epithelial malignant cells expressing Epstein-Barr virus latent **infection** protein
AUTHOR(S): Imai, Shosuke; Koizumi, Shigeki; Sugiura, Makoto; Tokunaga, Masayoshi; Uemura, Yoshiko; Yamamoto, Noriko; Tanaka, Sadao; Sato, Eiichi; Osato, Toyoro
CORPORATE SOURCE: Sch. Med., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(19), 9131-5
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In 1000 primary gastric carcinomas, 70 (7.0%) contained Epstein-Barr virus (EBV) genomic sequences detected by PCR and Southern blots. The pos. tumors comprised 8 of 9 (89%) undifferentiated lymphoepithelioma-like carcinomas, 27 of 476 (5.7%) poorly differentiated adenocarcinomas, and 35 of 515 (6.8%) moderately to well-differentiated adenocarcinomas. In situ EBV-encoded small RNA 1 **hybridization** and hematoxylin/eosin staining in adjacent sections showed that the EBV was present in every carcinoma cell but was not significantly present in lymphoid stroma and in normal mucosa. Two-color immunofluorescence and hematoxylin/eosin staining in parallel sections revealed that every keratin-pos. epithelial malignant cell expressed EBV-detd. nuclear antigen 1 (EBNA1) but did not significantly express CD45+ infiltrating leukocytes. A single fused terminal fragment was detected in each of the EBNA1-expressing tumors, thereby suggesting that the EBV-carrying gastric carcinomas

represent clonal proliferation of cells infected with EBV. The carcinoma cells had exclusively EBNA1 but not EBNA2, -3A, -3B, and -3C; leader protein; and latent membrane protein 1. The patients with EBV-carrying gastric carcinoma had elevated serum EBV-specific antibodies. The EBV-specific cellular immunity was not significantly reduced; however, the **cytotoxic T-cell** target antigens were not expressed. These findings strongly suggest a causal relation between a significant proportion of gastric carcinoma and EBV, and the virus-carrying carcinoma cells may evade immune surveillance.

L6 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:252437 HCAPLUS
DOCUMENT NUMBER: 118:252437
TITLE: Interferon-inducible gene expression in chimpanzee liver infected with hepatitis C virus
AUTHOR(S): Kato, Tamami; Esumi, Mariko; Yamashita, Susumu; Abe, Kenji; Shikata, Toshio
CORPORATE SOURCE: Sch. Med., Nihon Univ., Tokyo, 173, Japan
SOURCE: Virology (1992), 190(2), 856-60
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mol. host response to hepatitis C virus (HCV) **infection** was examd. by isolation of HCV-induced genes from a cDNA library constructed from chimpanzee liver during the acute phase of hepatitis C. Two cDNA clones, 130-7 and 130-51, were obtained by differential **hybridization** with cDNA probes prepd. from poly(A)+ RNAs of infected and uninfected livers. Northern blot anal. revealed that the 130-7 and 130-51 cDNAs were expressed as 1.5- and 1.0-kb products, resp., in chimpanzee liver and that the induction rates of the two were 20 and 4, resp. Nucleotide sequence analyses of these cDNA inserts showed that the sequence of cDNA 130-7 was that of a class I major histocompatibility antigen and that the sequence of cDNA 130-51 was 98% homologous with a human interferon-inducible mRNA. These results suggest that HCV **infection** may actively induce interferon, which in turn induces the expressions of these interferon-inducible genes. Furthermore, the high expression of HLA class I antigen in the acute phase of hepatitis C suggests that liver cell injury in HCV **infection** may be mediated by **cytotoxic T cells** that recognize viral antigen in assocn. with HLA class I antigen.

L6 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:100253 HCAPLUS
DOCUMENT NUMBER: 118:100253
TITLE: Epstein-Barr virus and Hodgkin's disease: Transcriptional analysis of virus latency in the malignant cells
AUTHOR(S): Deacon, E. M.; Pallesen, G.; Niedobitek, G.; Crocker, J.; Brooks, L.; Rickinson, A. B.; Young, L. S.
CORPORATE SOURCE: Med. Sch., Univ. Birmingham, Birmingham, B15 2TJ, UK
SOURCE: Journal of Experimental Medicine (1993), 177(2), 339-49
CODEN: JEMEAV; ISSN: 0022-1007

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Epstein-Barr virus (EBV) is assocd. with a no. of different human tumors and appears to play different pathogenetic roles in each case. Thus, immunoblastic B cell lymphomas of the immunosuppressed display the full pattern of EBV latent gene expression (expressing Epstein-Barr nuclear antigen [EBNA]1, 2, 3A, 3B, 3C, and -LP, and latent membrane protein [LMP]1, 2A, and 2B), just as do B lymphoblastoid cell lines transformed by the virus in vitro. In contrast, those EBV-assocd. tumors with a more complex, multistep pathogenesis show more restricted patterns of viral gene expression, limited in Burkitt's lymphoma to EBNA1 only and in nasopharyngeal carcinoma (NPC) to EBNA1 and LMP1, 2A, and 2B. Recent evidence has implicated EBV in the pathogenesis of another lymphoid tumor, Hodgkin's disease (HD), where the malignant Hodgkin's and Reed-Sternberg (HRS) cells are EBV genome pos. in up to 50% of cases. Here preliminary results are extended on viral gene expression in HRS cells by adopting polymerase chain reaction-based and in situ **hybridization** assays capable of detecting specific EBV latent transcripts diagnostic of the different possible forms of EBV latency. The transcriptional program of the virus in HRS cells is similar to that seen in NPC in several respects: (a) selective expression of EBNA1 mRNA from the BamHI F promoter: (b) downregulation of the BamHI C and W promoters and their assocd. EBNA mRNAs; (c) expression of LMP1 and, in most cases, LMP2A and 2B transcripts; and (d) expression of the rightward-running BamHI A transcripts once thought to be unique to NPC. This form of latency, consistently detected in EBV-pos. HD irresp. of histol. subtype, implies an active role for the virus in the pathogenesis of HD and also suggests that the tumor may remain sensitive to at least certain facets of the EBV-induced **cytotoxic T cell** response.

L6 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:19650 HCAPLUS
DOCUMENT NUMBER: 116:19650
TITLE: Intracellular antigen found in subpopulation of CD8+ T-lymphocytes and monoclonal antibody reactive with same
INVENTOR(S): Anderson, Paul J.; Streuli, Michel; Schlossman, Stuart F.
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 436400	A1	19910710	EP 1990-314456	19901231
EP 436400	B1	19990825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5079343	A	19920107	US 1990-460678	19900105
JP 05184387	A2	19930727	JP 1990-415435	19901228
AT 183777	E	19990915	AT 1990-314456	19901231
CA 2033644	AA	19910706	CA 1991-2033644	19910104

PRIORITY APPLN. INFO.: US 1990-460678 19900105

AB A 15-kilodalton (kd) protein antigen (TIA-1 antigen) is assocd. with cytoplasmic granules in cytolytic T-lymphocytes and natural killer cells. Monoclonal antibodies immunol. reactive with TIA-1 antigen, and nucleic acid probes encoding polypeptides that are immunol. cross-reactive with TIA-1 antigen, can be used to identify cytolytic lymphocytes in a sample and provide early warning of **infections**. Thus, mice were immunized with digitonin-permeabilized T-lymphocytes, and their splenocytes were subsequently fused with NS-1 myeloma cells. The hybridoma cells were cloned and screened with permeabilized T-lymphocytes by flow cytometry. TIA-1 antigen was expressed by 55% of CD8+ cells and 6% of CD4+ cells, but not by immortalized T-cell lines or by B-cells. TIA-1 antigen did not have serine protease activity. A .lambda. gt11 cDNA library, prepd. from RNA isolated from a **cytotoxic T-cell** clone, was subjected to immunoscreening using TIA-1, and a cloned recombinant cDNA encoding the TIA-1 antigen was sequenced.

L6 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:512596 HCAPLUS

DOCUMENT NUMBER: 115:112596

TITLE: Mutational analysis of regulation of MHC and antiviral genes

AUTHOR(S): Rodgers, John R.; Wyde, Philip R.; Rich, Robert R.

CORPORATE SOURCE: Dep. Immunol. Microbiol., Baylor Coll. Med., Houston, TX, 77030, USA

SOURCE: Journal of Immunology (1991), 146(6), 1979-86
CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Cytotoxic T-lymphocyte** mediated selection for loss of expression of Mta by H-2-heterozygous SV40-transformed mouse fibroblasts (line 24SV) produced an unusual phenotypic class of maternally transmitted antigen (Ag) neg. mutants defective in both MHC expression and in anti-viral activity. Severely reduced surface expression of class I MHC Ag from multiple loci of both haplotypes correlated with low levels of MHC H chain and .beta.2-microglobulin mRNA. Inasmuch as IFN can up-regulate class I expression and some fibroblasts elaborate autocrine IFN-.beta., the authors examd. whether IFN could restore wild-type expression of class I MHC Ag. However, IFN could not restore wild-type expression. Moreover, the fold-increases in class I Ag and mRNA expression were significantly reduced in mutant cells compared to wild-type cells. These results suggested that the mutants might have generalized defects in IFN response. Inasmuch as the induction of an anti-viral state is a hallmark of IFN responses, the authors exposed cells to IFN-.alpha., -.beta., or -.gamma. and challenged with virus. 24SV cells, exposed to any of the three IFNs, were completely protected from destruction by vesicular stomatitis, mengovirus or respiratory syncytial viruses. In contrast, MHC and anti-viral defective mutants could not be protected from virus-induced lysis by any IFN. Somatic cell **hybridization** analyses indicated that both basal MHC and IFN-inducible phenotypes were recessive to wild-type, and that a trans-acting regulatory factor required for basal MHC expression is defectively expressed in the mutants. Such a factor may integrate

the organismal response to virus **infection**, encompassing both immune and nonimmune anti-viral responses.

L6 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:512529 HCAPLUS
DOCUMENT NUMBER: 115:112529
TITLE: The role of CD4+ cells in sustaining lymphocyte proliferation during lymphocytic choriomeningitis virus **infection**
AUTHOR(S): Kasaian, Marion T.; Leite-Morris, Kimberly A.; Biron, Christine A.
CORPORATE SOURCE: Div. Biol. Med., Brown Univ., Providence, RI, 02912, USA
SOURCE: Journal of Immunology (1991), 146(6), 1955-63
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The murine immune response to lymphocytic choriomeningitis virus [LCMV] **infection** involves the activation of CD8+, class I MHC-restricted and virus-specific **CTL**. At times coinciding with **CTL** activation, high levels of IL-2 gene expression and prodn. occur, the IL-2R is expressed, and T cell blastogenesis and proliferation are induced. Although both CD4+ and CD8+ T cell subsets transcribe IL-2, the CD4+ subset appears to be the major producer of IL-2 whereas the CD8+ subset appears to be the major proliferating population when the subsets are sepd. after activation in vivo. The studies presented here were undertaken to examine the contribution made by the CD4+ subset to lymphocyte proliferation in vivo. Responses to LCMV **infection** were examd. in intact mice and in mice depleted of CD4+ or CD8+ subsets by antibody **treatments** in vivo. Protocols were such that in vivo **treatments** with anti-CD4 or anti-CD8 depleted the resp. subset by >90%. In situ **hybridizations** demonstrated that the IL-2 gene was expressed in non-B lymphocytes isolated from either CD4+ cell-depleted or CD8+ cell-depleted mice on day 7 post-**infection** with LCMV. When placed in culture, however, cells from CD8+ cell-depleted mice produced higher levels of detectable IL-2 than did cells isolated from CD4+ cell-depleted mice on day 7 post-**infection**. IL-2 was apparently produced in vivo in mice depleted of either CD4+ or CD8+ cells, as expression of the gene for the p55 chain of the IL-2R, IL-2 responsiveness, and lymphocyte proliferation were obsd. with cells isolated from both sets of mice. Lymphocyte proliferation was shown to be sustained in mice depleted of CD4+ cells in vivo by three criteria: 1) non-B lymphocytes isolated from infected mice depleted of CD4+ cells underwent more DNA synthesis than did those isolated from uninfected mice or from infected mice depleted of CD8+ cells; 2) leukocyte yields were expanded during **infection** of CD4+ cell-depleted mice; and 3) CD8+ cell nos. were increased during **infection** of CD4+ cell-depleted mice. The majority of non-B lymphocytes having the characteristics of blast lymphocytes was recovered in the CD8+ populations isolated from infected CD4+ cell-depleted mice. These finding suggest that the requirement for the CD4+ subset to sustain CD8+ lymphocyte proliferation in vivo is limited, and that CD4+ and CD8+ cell types can function independently in many aspects of their responses to viral **infections**.

L6 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:151425 HCAPLUS
DOCUMENT NUMBER: 112:151425
TITLE: Effects of cyclosporin A on IL-2 production and lymphocyte proliferation during **infection** of mice with lymphocytic choriomeningitis virus
AUTHOR(S): Kasaian, Marion T.; Biron, Christine A.
CORPORATE SOURCE: Div. Biol. Med., Brown Univ., Providence, RI, 02912, USA
SOURCE: Journal of Immunology (1990), 144(1), 299-306
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The immunosuppressive agent, cyclosporin A (CsA) blocks prodn. of IL-2 by lymphocytes in vitro, and impairs immune responses in vivo. During **infection** of mice with lymphocytic choriomeningitis virus (LCMV), IL-2 is produced by spleen lymphocytes with a time course corresponding to that of T cell activation and proliferation, but distinct from NK cell activation and proliferation. To evaluate the requirement for IL-2 in supporting lymphocyte proliferation in vivo, and to investigate the mechanisms of CsA-induced immunosuppression, the effects of CsA on LCMV-elicited responses were examd. CsA had profound effects on lymphocyte expansion and **CTL** activation on day 7 postinfection, the peak of the T cell response to LCMV. Proliferation of both the CD4+ and CD8+ T cell subsets was affected. Inhibition of T cell expansion was accompanied by the inhibition of IL-2 prodn. and IL-2 responsiveness. In situ **hybridization** revealed a 50% redn. in the percentage of cells transcribing IL-2, suggesting that CsA blocked IL-2 prodn. at the level of gene transcription. Transcripts of the gene for the IL-2R p55 chain are also normally elevated during **infection**, and CsA **treatment** resulted in an 80% redn. in the percentage of cells transcribing this gene. A reduced responsiveness of freshly isolated cells to rIL-2 in vitro correlated with the redn. of IL-2 receptor gene transcription pos. cells. In contrast to effects of the drug on T cells, the level of NK cell activation was not decreased as a result of CsA **treatment**. These observations suggest that the IL-2 produced by lymphocytes in vivo in response to virus **infection** is required to promote the T cell response to LCMV, but do not support a role for IL-2 in NK cell activation under the conditions examd. Furthermore, the data demonstrate the profound inhibition of lymphocyte proliferation induced by CsA **treatment** during an in vivo immune response.

L6 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:592901 HCAPLUS
DOCUMENT NUMBER: 111:192901
TITLE: Detection of perforin and granzyme A mRNA in infiltrating cells during **infection** of mice with lymphocytic choriomeningitis virus
AUTHOR(S): Mueller, Christoph; Kaegi, David; Aebischer, Toni; Odermatt, Bernhard; Held, Werner; Podack, Eckhard R.; Zinkernagel, Rolf M.; Hengartner, Hans
CORPORATE SOURCE: Dep. Pathol., Univ. Bern, Bern, Switz.
SOURCE: European Journal of Immunology (1989), 19(7),

1253-9
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The anal. of gene expression in **cytotoxic T cells** by in situ **hybridization** of serial liver and brain sections from mice infected with lymphocytic choriomeningitis virus (LCMV) and immunostaining with T cell marker- and virus-specific antibodies revealed a close histol. assocn. of infiltrating lymphocytes expressing the perforin and granzyme A genes with virally infected cells. Maximal frequency of perforin and granzyme A mRNA-contg. cells on liver sections preceded by about 2 days maximal LCMV-specific cytotoxicity of the lymphoid liver infiltrating cells. These results are most consistent with an involvement of perforin and granzyme A in cell-mediated cytotoxicity in vivo.

L6 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:628438 HCAPLUS
DOCUMENT NUMBER: 109:228438
TITLE: Immunization with solid matrix-antibody-antigen complexes containing surface or internal virus structural proteins protects mice from **infection** with the paramyxovirus, simian virus 5
AUTHOR(S): Randall, R. E.; Young, D. F.; Southern, J. A.
CORPORATE SOURCE: Dep. Biochem. Microbiol., Univ. St. Andrews, St. Andrews/Fife, KY16 9AL, UK
SOURCE: Journal of General Virology (1988), 69(10), 2517-26
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A mouse model system was developed to examine the ability of purified virus proteins to protect mice from **infection** with the paramyxovirus simian virus 5. The system is based on the **infection** of mouse lungs by intranasal administration of **infectious** virus. The relative amts. of virus proteins and nucleic acid present within infected lungs were estd. either by Western blot anal. of disrupted lung tissues or by in situ **hybridization** studies using cryostat sections of infected lungs. During a normal time course of **infection** in non-immunized mice increasing amts. of virus protein and nucleic acid were detected in the lungs until 3 days post-**infection** (p.i.). Thereafter the amt. of virus present within the lungs remained relatively const. until 7 days p.i. when there was a rapid decrease. **Cytotoxic T cells**, but not neutralizing antibody, could be detected at the time when the amt. of virus within the lungs was decreasing. Prior immunization of mice with solid matrix-antibody-antigen (SMAA) complexes contg. either surface or internal virus structural proteins reduced the amt. of virus replication within infected lungs, the greatest degree of protection being obsd. when nucleoprotein or matrix protein was used to immunize the mice. There was no correlation between the degree of protection obsd. and the level of neutralizing antibody present in immunized animals; no neutralizing antibody was detected in mice immunized with internal virus proteins even at the time of sacrifice 5 days p.i. It was previously shown that immunization of

mice with SMAA complexes contg. either surface or internal virus structural proteins can induce **cytotoxic T cells** so the most likely explanation for the protection obsd. in immunized mice is through the induction of **cytotoxic T cells**.

L6 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:174274 HCAPLUS
DOCUMENT NUMBER: 106:174274
TITLE: Epstein-Barr virus-specific T-cell recognition of B-cell transformants expressing different EBNA 2 antigens
AUTHOR(S): Wallace, L. E.; Young, L. S.; Rowe, M.; Rowe, D.; Rickinson, A. B.
CORPORATE SOURCE: Med. Sch., Univ. Birmingham, Birmingham, B15 2TJ, UK
SOURCE: International Journal of Cancer (1987), 39(3), 373-9
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epstein-Barr (EB) virus isolates can be classified as type A or type B depending upon the identity of the virus-encoded nuclear antigen EBNA 2. The EBNA 2A and 2B proteins show limited amino-acid homol. and induce largely non-cross-reactive antibody responses in humans. To examine whether EBNA 2 might also be a target for virus-specific **cytotoxic T-cell** responses (like intracellular antigens in other viral systems), normal B cells from non-immune donors of known HLA type were transformed in vitro with virus isolates either of type A (from the B95-8 and IARC-BL74 cell lines) or of type B (from the AG876 and IARC-BL16 cell lines) to provide a suitable panel of target cells. DNA **hybridization** with type-specific probes and immunoblotting with type-specific antisera confirmed the EBNA 2 type of the resident virus in the various in vitro transformants. These cells were then tested as targets for virus-specific **cytotoxic T cells**, the latter being prepd. from type-A virus-infected donors by in vitro reactivation of memory cells from peripheral blood using autologous type-A virus-transformed cells as stimulators. Such effector cells lysed type-A virus-transformed and type-B virus-transformed target cells equally well, indicating that EBNA 2 (in particular that part of the protein which varies between virus types) seems not to be a dominant antigen for the induction of EB virus-specific cytotoxic responses.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:44:16 ON 13 DEC 2002)
L1 15825 SEA FILE=HCAPLUS ABB=ON PLU=ON CTL OR CYTOTOX?(W)T(W)(LYMPHOCYT? OR CELL)
L2 4228 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND (INFECTIO## OR HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W)SYNDROM?)
L8 1 SEA L2 AND (SUBSTRACT?(W)(HYBRIDIS? OR HYBRIDIZ?) OR (MICROARRAY? OR MICRO ARRAY?)(5A)(NUCLEIC OR DEOXYRIBONUCLEIC OR DEOXY RIBONUCLEIC OR DNA))

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L1        15825 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CTL OR CYTOTOX?(W)T(W)(L
                YMPHOCYT? OR CELL)
L2         4228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND (INFECTIO## OR
                HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W)SYND
                ROM?)
L5           24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 AND (HYBRIDIS? OR
                HYBRIDIZ? OR MICROARRAY? OR MICRO ARRAY?)
L7          306 SEA L5
L9          156 SEA L7 AND (SCREEN? OR DETERM? OR DETECT? OR DET##)
L10          46 SEA L9 AND (THERAP? OR TREAT? OR IMMUNOGEN?)

L11          46 L8 OR L10


PROCESSING COMPLETED FOR L11
L12          37 DUP REM L11 (9 DUPLICATES REMOVED)

L12  ANSWER 1 OF 37  WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER:     2002-315804 [35]   WPIDS
DOC. NO. CPI:         C2002-092032
TITLE:                Screening for therapeutics
                      (e.g. antigens for use in vaccines) for
                      infectious diseases such as viral
                      infections, by identifying
                      immunogenic host cell gene products which
                      are upregulated or expressed only during
                      infection.
DERWENT CLASS:        B04 D16
INVENTOR(S):          ZAUDERER, M
PATENT ASSIGNEE(S):   (UYRP) UNIV ROCHESTER
COUNTRY COUNT:        97
PATENT INFORMATION:

     PATENT NO   KIND DATE     WEEK      LA   PG
     -------------------------------------------
     WO 2002027027 A2 20020404 (200235)* EN   42
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
            MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ
            DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
            KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
            NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG
            US UZ VN YU ZA ZW
     AU 2001094831 A  20020408 (200252)

APPLICATION DETAILS:

     PATENT NO   KIND                  APPLICATION      DATE
     ------------------------------------------------------------
     WO 2002027027 A2                  WO 2001-US30334  20011001
     AU 2001094831 A                   AU 2001-94831    20011001

FILING DETAILS:

     PATENT NO   KIND                  PATENT NO
     ---------------------------------------------
     AU 2001094831 A  Based on         WO 200227027
```

PRIORITY APPLN. INFO: US 2000-236381P 20000929
AN 2002-315804 [35] WPIDS
AB WO 200227027 A UPAB: 20020603
NOVELTY - A new method (M1) for **screening** for **therapeutics** for **infectious** diseases, comprising identifying host cell gene products which are upregulated or expressed only during **infection, screening** the products for **immunogenicity** and **determining** which products are **immunogenic.**
ACTIVITY - Immunostimulant; antibacterial; antiparasitic; antiviral; antifungal.
No suitable biological data given.
MECHANISM OF ACTION - Vaccine.
No suitable biological data given.
USE - The method is useful for **screening** for **therapeutics** (e.g. antigens for use in vaccines) for **infectious** diseases such as viral, fungal, bacterial or parasitic **infections.**
Dwg.0/1

L12 ANSWER 2 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-339446 [37] WPIDS
CROSS REFERENCE: 2002-241837 [29]
DOC. NO. CPI: C2002-097458
TITLE: Novel hepatitis C virus NS3/4A peptide useful for diagnosing presence or absence of hepatitis C virus in a subject and for preparing a medicament for **treating** hepatitis C virus **infection.**
DERWENT CLASS: B04 D16
INVENTOR(S): SALLBERG, M
PATENT ASSIGNEE(S): (TRIP-N) TRIPEP AB
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002014362	A2	20020221	(200237)*	EN	90
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001090178	A	20020225	(200245)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002014362	A2	WO 2001-IB1774	20010815
AU 2001090178	A	AU 2001-90178	20010815

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2001090178 A Based on WO 200214362

PRIORITY APPLN. INFO: US 2000-705547 20001103; US 2000-225767P 20000817; US 2000-229175P 20000829

AN 2002-339446 [37] WPIDS

CR 2002-241837 [29]

AB WO 200214362 A UPAB: 20020717

NOVELTY - A purified or isolated hepatitis C virus (HCV) NS3/4A peptide (I) consisting:

(a) essentially of a fully defined sequence of 686 amino acids (S2) as given in specification;

(b) consisting any one of the 9 fully defined mutant HCV NS3/4A peptide sequences of 686 amino acids (S3-S11) as given in the specification; or

(c) comprising a sequence of (S2), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a purified or isolated nucleic acid (II) consisting of or consisting essentially of a fully defined sequence of 2061 nucleotides (S1) as given in the specification;

(2) a purified or isolated fragment (III) of (II) of sequence (S1), where the fragment consists of at least 9 consecutive nucleotides;

(3) a purified or isolated nucleic acid (IV) encoding a peptide of sequence (S2-S11);

(4) a fragment (V) of (IV) which encodes a peptide having a fully defined sequence of TKYMTCMSADLEVVTSTWVLVGGVL, SADLEVVTSTWV, TKYMTCMSADLEVVTGTWVLVGGVL, TKYMTCMSADLEVVRTWVLVGGVL, TKYMTCMSADLEVVTPPWVLVGGVL, TKYMTCMSADLEVVRPTWVLVGGVL, TKYMTCMSADLEVVRPAWVLVGGVL, TKYMTCMSADLEVVCSTWVLVGGVL, TKYMTCMSADLEVCCSTWVLVGGVL, TKYMTCMSADLEVSSSTWVLVGGVL, TKYMTCMSADSSSSCSTWVLVGGVL TKYMTCMSADVVVVTSTWVLVGGVL, SSEDVVCCSMWVLVGGVL (S14-S26);

(5) a vector (VI) comprising (II)-(V);

(6) a cell (VII) comprising (II)-(V);

(7) a purified or isolated fragment (VIII) of (I) consisting of a sequence of (S2), where the fragment consists of 9 consecutive nucleotides;

(8) a fragment (IX) of (I) consisting of a sequence of (S2-S11), where the fragment comprises a sequence of (S14)-(S26);

(9) an isolated or purified antibody (X) that directly interacts with one of (I), (VIII) or (IX); and

(10) a medicament (XI) comprising (I), (II), (III), (IV), (V), (VIII), or (IX).

ACTIVITY - Virucide.

MECHANISM OF ACTION - Vaccine.

To examine whether a T-cell response was elicited by the NS3/4A immunization, the capacity of an immunized mouse's immune defense system to attack the NS3-expressing tumor cell line was assayed. Groups of ten mice were immunized i.m. five times with one month intervals with either 100 micro g NS3-pVAX or 100 micro g NS3/4A-pVAX. Two weeks after the last immunization 2 multiply 106 SP/0 or N3/4A-SP2/0 cells were injected into the right flank of each mouse. Two weeks later the mice were sacrificed and the maximum tumor sizes were measured. There was no difference between the mean SP2/0 and NS3/4A-SP2/0 tumor sizes in the NS3-pVAX immunized mice. Also the inhibition of SP2/0 or NS3/4A-SP2/0 tumor growth was evaluated in NS3/4A-pVAX immunized Balb/c mice. In mice immunized

with the NS3/4A-pVAX plasmid the growth of NS3/4-SP2/0 tumor cells was significantly inhibited as compared to growth of the non-transfected SP2/0 cells. Thus NS3/4A-pVAX immunization elicited **cytotoxic T lymphocytes (CTLs)** that inhibited growth of cells expressing NS3/4A in vivo.

USE - (II)-(V) or (V) is useful for identifying the presence or absence of hepatitis C virus in a subject which involves contacting (II)-(IV) or (V) with a target nucleic acid obtained from a biological sample of the subject under conditions that permit **hybridization**; and **detecting** the presence or absence of a nucleic acid hybrid consisting of the nucleic acid and the target nucleic acid, whereby the presence or absence of hepatitis C virus in the subject is identified. Prior to **detection** the method involves amplifying at least a fragment of the target nucleic acid. (X) is also useful for diagnosing presence or absence of HCV in a subject which involves contacting (X) with a peptide obtained from a biological sample of the subject under conditions that permit binding and **detecting** the presence or absence of biological complex consisting of antibody and peptide, whereby the presence or absence of HCV in the subject is identified. The peptides (I), (VIII) or (IX) are also useful for diagnosing the presence or absence of HCV in a subject, where the peptide is contacted with biological sample of subject or antibodies obtained from biological sample under conditions that permit binding and **detecting** presence or absence of biological complex consisting of peptide and antibody, whereby the presence or absence of HCV in the subject is identified. (XI) is useful for **treating** or preventing HCV **infection** (all claimed).

Dwg.0/5

L12 ANSWER 3 OF 37 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-179901 [23] WPIDS

CROSS REFERENCE: 2000-431303 [37]; 2001-374831 [39]

DOC. NO. CPI: C2002-055975

TITLE: Novel compositions comprising Chlamydia Capl protein and its use in the **treatment** of Chlamydia **infection**.

DERWENT CLASS: B04 D16

INVENTOR(S): BHATIA, A; PROBST, P; SKEIKY, Y A W; FLING, S P

PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP; (BHAT-I) BHATIA A; (PROB-I) PROBST P; (SKEI-I) SKEIKY Y A W

COUNTRY COUNT: 96

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002008267	A2	20020131	(200223)*	EN	526
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001080702	A	20020205	(200236)		
US 2002061848	A1	20020523	(200239)		
US 6448234	B1	20020910	(200263)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002008267	A2		WO 2001-US23121	20010720
AU 2001080702	A		AU 2001-80702	20010720
US 2002061848	A1	CIP of	US 2000-620412	20000720
			US 2001-841132	20010423
US 6448234	B1	CIP of	US 1998-208277	19981208
		CIP of	US 1999-288594	19990408
		CIP of	US 1999-410568	19991001
		CIP of	US 1999-426571	19991022
		CIP of	US 1999-454684	19991203
		CIP of	US 2000-556877	20000419
		CIP of	US 2000-598419	20000620
			US 2000-620412	20000720

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001080702	A	Based on	WO 200208267
US 6448234	B1	CIP of	US 6166177

PRIORITY APPLN. INFO: US 2001-841132 20010423; US 2000-620412 20000720; US 1998-208277 19981208; US 1999-288594 19990408; US 1999-410568 19991001; US 1999-426571 19991022; US 1999-454684 19991203; US 2000-556877 20000419; US 2000-598419 20000620

AN 2002-179901 [23] WPIDS
CR 2000-431303 [37]; 2001-374831 [39]
AB WO 200208267 A UPAB: 20021007
NOVELTY - Novel compositions comprising a Chlamydia Cap1 protein and methods for the diagnosis and **therapy** of Chlamydia **infection.**

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a composition (C1) for eliciting an immune response comprising a Chlamydia Cap1 protein or an **immunogenic** fragment and an immunostimulant;

(2) a composition (C2) for eliciting an immune response comprising an isolated polynucleotide that encodes a Chlamydia Cap1 protein or an **immunogenic** fragment and an immunostimulant;

(3) a method (M1) for stimulating a Chlamydia-specific T-cell response and/or inhibiting the development of a Chlamydia **infection** in an animal, comprising administering (C1) or (C2);

(4) an isolated polynucleotide (I) comprising a sequence selected from:

(a) four fully defined sequences (S1) of 1248, 1311, 813 and 750 base pairs given in the specification;

(b) complements of (S1);

(c) sequences consisting of at least 20 contiguous residues of (S1);

(d) sequences that **hybridize** to (S1), under highly stringent conditions;

(e) sequences that have at least 95%, preferably 99% identity to one of (S1); and

(f) degenerate variants of (S1);

(5) an isolated polypeptide (II) comprising an amino acid sequence selected from:

(a) sequences encoded by (I);

(b) sequences having at least 95%, preferably 99% identity to (II)

(6) an isolated polypeptide (III) comprising at least an **immunogenic** fragment of a polypeptide sequence selected from:

(a) four fully defined sequences (S2) of 412, 433, 264 and 249 amino acid residues given in the specification;

(b) a polypeptide sequence having at least 95%, preferably 99% identity to one of (S2);

(7) an expression vector (IV) comprising (I) operably linked to an expression control sequence;

(8) a host cell transformed or transfected with (IV);

(9) an isolated antibody or antigen-binding fragment that specifically binds to (II) and (III);

(10) a method (M2) for **detecting** the presence of Chlamydia in a patient;

(11) a fusion protein comprising (II) or (III);

(12) an oligonucleotide that **hybridizes** to one of (S1);

(13) a method (M3) for stimulating and/or expanding T cells specific for a Chlamydia protein, comprising contacting the T cells with at least one component;

(14) an isolated T cell population, comprising T cells prepared according to (M3);

(15) a composition (C3) comprising a first compound selected from physiologically acceptable carriers and immunostimulants and a second group;

(16) a method (M4) of stimulating an immune response in a patient, comprising administering a composition;

(17) methods (M5) for the **treatment** of Chlamydia **infection** in a patient;

(18) method (M6) for determining the presence of Chlamydia in a patient; and

(19) a diagnostic kit comprising at least one oligonucleotide that hybridizes to one of (S1).

ACTIVITY - Antibacterial; immunostimulant.

C3H mice (4 mice per group) were immunized three times with 50 micro g of pcDNA-3 expression vector containing C. trachomatis SWIB DNA (a fully defined 481 base pairs sequence and its corresponding 86 amino acid sequence protein given in the specification) encapsulated in poly lactitide co-glycolide microspheres (PLG); immunizations were made intra-peritoneally. Two weeks after the last immunization, animals were progesterone treated and infected by inoculation of C. pisttaci in the vagina. Two weeks after the infection, mice were sacrificed and genital tracts sectioned, stained and examined for histopathology. Inflammation level was scored from mild (+) to very severe (+++++). Scores attributed to each single oviduct/ovary were summed and divided by the number of examined organs to get a mean inflammation for the group. Negative control-immunized animals receiving a PLG-encapsulated empty vector showed consistent inflammation with an ovary/oviduct mean inflammation score of 7.28, versus 5.71 for the PLG-encapsulated DNA

immunized group. Inflammation in the peritoneum was 1.75 for the vaccinated group versus 3.75 for the control.

MECHANISM OF ACTION - Vaccine.

USE - C1 and C2 are useful for eliciting an immune response, specifically stimulating a Chlamydia-specific T-cell response or inhibiting the development of a Chlamydia infection in an animal. (M2) is useful for detecting the presence of Chlamydia in a patient and (M3) can be used to stimulate and/or expand T cells specific for a Chlamydia protein. (M5) are useful for treatment of a Chlamydia infection (claimed).

Dwg.0/12

L12 ANSWER 4 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-188381 [24] WPIDS
DOC. NO. CPI: C2002-058183
TITLE: New isolated or recombinant promoter/enhancers, useful in producing a prophylactic or **therapeutic** effect in humans, especially useful in gene **therapy** for **treating** or preventing **infectious** diseases, autoimmune disorders or tumors.
DERWENT CLASS: B04 D16
INVENTOR(S): PUNNONEN, J; SEMYONOV, A; WRIGHT, A
PATENT ASSIGNEE(S): (MAXY-N) MAXYGEN INC; (PUNN-I) PUNNONEN J; (SEMY-I) SEMYONOV A; (WRIG-I) WRIGHT A
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002000897	A2	20020103	(200224)*	EN	119
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001068716	A	20020108	(200235)		
US 2002081708	A1	20020627	(200245)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002000897	A2	WO 2001-US20123	20010621
AU 2001068716	A	AU 2001-68716	20010621
US 2002081708	A1 Provisional	US 2000-213829P	20000623
		US 2001-886942	20010621

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001068716	A Based on	WO 200200897

PRIORITY APPLN. INFO: US 2000-213829P 20000623; US 2001-886942 20010621

AN 2002-188381 [24] WPIDS
AB WO 200200897 A UPAB: 20020416
NOVELTY - An isolated or recombinant nucleic acids, which comprise any of 18 sequences fully defined in the specification, is new. The nucleic acids are designated 10B2, 11E2, 12C9, 12E1, 12H9, 3C9, 4B5, 6A8, 6B2, 6D4, 6F6, 9E1, 9F11, 9G11, 9G12, 9G4, 9G7 and 9G8, and comprise 898-1768 base pair sequences.

DETAILED DESCRIPTION - An isolated or recombinant nucleic acids comprise a polynucleotide sequence:

(a) consisting of any of the 18 sequences, designated 10B2, 11E2, 12C9, 12E1, 12H9, 3C9, 4B5, 6A8, 6B2, 6D4, 6F6, 9E1, 9F11, 9G11, 9G12, 9G4, 9G7 or 9G8, or their complementary polynucleotide sequence;

(b) that has at least 97 % sequence identity to at least one sequence of (a);

(c) that has at least 80 % sequence identity to at least one sequence from (a), where the polynucleotide sequence promotes expression of an operably linked transgene at a level that is greater than the level of expression of the same transgene when operably linked to a human cytomegalovirus (CMV) promoter polynucleotide sequence;

(d) comprising a fragment of (a)-(c), where the fragment promotes expression of an operably linked transgene at a level that is greater than the level of expression of the same transgene when operably linked to a human CMV promoter polynucleotide sequence;

(e) comprising a fragment of one sequence from (a), where the fragment comprises a unique subsequence; or

(f) that **hybridizes** under highly stringent conditions over substantially the entire length of (a)-(e).

INDEPENDENT CLAIMS are also included for the following:

(1) a method of producing a polypeptide, comprising:

(a) providing a population of cells comprising the nucleic acid operably linked to a transgene encoding a polypeptide; and

(b) expressing the polypeptide in at least the subset of the population of cells or their progeny;

(2) a method of producing a modified or recombinant nucleic acid by mutating or recombining the nucleic acids;

(3) a nucleic acid library produced by the method of (2), or comprising two or more of the novel nucleic acids;

(4) a vector comprising at least one of the novel nucleic acids;

(5) a cell comprising the novel nucleic acid or the vector of (4);

(6) a population of cells comprising the library of (3);

(7) compositions produced by:

(a) the cleaving of one or more of the novel nucleic acids, where the cleaving comprises mechanical, chemical or enzymatic cleavage; or

(b) by incubating one or more of the novel nucleic acids in the presence of deoxyribonucleotide triphosphates and a nucleic acid polymerase;

(8) compositions comprising the novel nucleic acids or the vector of (3), and a carrier;

(9) kits comprising the novel nucleic acid or the vector of (3);

(10) database comprising one or more character strings corresponding to:

(a) any of the novel nucleic acids; or

(b) a unique subsequence of the polynucleotide sequence of (a) or a unique subsequence of a complementary polynucleotide sequence of them; and

(11) methods for manipulating a sequence record in a computer system comprising:

(a) reading a character string corresponding to the novel nucleic acid;

(b) performing an operation on the character string; and

(c) returning a result of the operation.

ACTIVITY - Immunomodulator; Cytostatic; Antibacterial.

No biological data is given.

MECHANISM OF ACTION - Gene therapy; DNA vaccine.

USE - The nucleic acids are useful in producing an immunogenic effect, a prophylactic effect or a therapeutic effect in a subject, particularly a human (claimed). The nucleic acids are particularly useful in genetic (DNA) vaccination or gene therapy, e.g. for treating or preventing infectious diseases, autoimmune disorders or tumors. The nucleic acids are also useful for directing gene expression, particularly the levels of gene expression, in mammalian cells. The nucleic acids may also be used for producing any polypeptide of interest for research, medical or industrial use.

Dwg.0/10

L12 ANSWER 5 OF 37 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-415200 [44] WPIDS

DOC. NO. CPI: C2002-117182

TITLE: New recombinant virus, useful for immunizing felines to prevent or **treat** feline immunodeficiency virus, comprises foreign nucleic acid encoding feline **cytotoxic T lymphocyte** accessory molecules CD28, CD80, CD86 or CTLA-4.

DERWENT CLASS: B04 C06 D16

INVENTOR(S): COCHRAN, M D; WINSLOW, B J

PATENT ASSIGNEE(S): (COCH-I) COCHRAN M D; (WINS-I) WINSLOW B J

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002051792	A1	20020502	(200244)*		77

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002051792	A1 Provisional	US 1998-83870P	19980501
		US 1999-303040	19990430

PRIORITY APPLN. INFO: US 1998-83870P 19980501; US 1999-303040 19990430

AN 2002-415200 [44] WPIDS

AB US2002051792 A UPAB: 20020711

NOVELTY - A recombinant virus comprising at least one foreign nucleic acid encoding a protein inserted within a non-essential region of the viral genome, the protein being selected from feline **cytotoxic T lymphocyte** accessory

molecules CD28, CD80, CD86 or CTLA-4 proteins or their **immunogenic** portions and being capable of expression when the virus is introduced into an appropriate host, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a virus as above further comprising a foreign nucleic acid encoding an **immunogen** derived from a pathogen;

(2) vaccines comprising an immunizing amount of virus or virus as in (1) and a carrier;

(3) enhancing an immune response in a feline comprising administering the recombinant virus;

(4) immunizing a feline comprising administering the recombinant virus;

(5) suppressing an immune response in a feline comprising administering the recombinant virus;

(6) reducing or abrogating a tumor in a feline comprising administering the recombinant virus, where the nucleic acid encodes a feline CD80 protein and/or CD86 protein; and

(7) suppressing an immune response in a feline by administering antisense nucleic acid **hybridizing** to and inhibiting translation of a feline CD28, CD80 or CD86 mRNA transcript.

ACTIVITY - Virucide; Immunostimulant; Immunosuppressive; Cytostatic. Recombinant viral vectors derived from feline herpes virus, swine pox virus or raccoon pox virus expressing pairwise combinations CD80 and CD28, CD80 and CTLA-4, CD86 and CD28 or CD86 and CTLA-4 or alternatively expressing all four molecules were constructed by known methods. Vectors were administered orally/intramuscularly to 8-week-old cats at 0.1-10 mg/kg body weight or 10 to the power of 4 to 10 to the power of 9 plaque forming units. A subunit or viral vector vaccine for feline immunodeficiency virus (FIV) or feline leukemia virus (FeLV) was administered simultaneously at minimum protective dose. At 3-4 weeks, cats received a second vaccine dose and were challenged with virulent FIV strain PPR or petaluma or FeLV Pickard strain conventionally. Cats were observed for 12 weeks for development of viremia; 60 % of Control cats (no vaccine) developed persistent viremia, whilst 75 % of those receiving subunit FIV/FeLV vaccine and 100 % of those receiving FIV/FeLV plus CD80, CD86, CD28 and CTLA-4 vaccine were protected against viremia.

MECHANISM OF ACTION - Vaccine; Antisense gene **therapy**.

USE - The virus or virus as in (1) can be administered (e.g. intravenously, subcutaneously etc.; claimed) to a feline to immunize the feline (claimed) or to enhance an immune response e.g. to prevent/**treat** feline immunodeficiency disease, feline leukemia, feline **infectious** peritonitis etc.. Viruses comprising nucleic acid encoding a feline CD80 protein and/or a feline CD86 protein may also be administered to reduce or abrogate tumors in felines, especially viruses further comprising an expressible feline tumor associated antigen and administered systemically. The viruses can also be included in vaccines useful as above. The viruses may also be administered to suppress an immune response e.g. to **treat** felines receiving a transplanted organ/tissue or suffering from an immune response (all claimed). An immune responses in a feline may also be suppressed by administering antisense nucleic acid **hybridizing** to and inhibiting translation of a feline CD28, CD80 or CD86 mRNA transcript as in (3).

Dwg.0/5

L12 ANSWER 6 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-239252 [29] WPIDS
DOC. NO. CPI: C2002-072121
TITLE: Representational Difference Analysis method for identification of antigens recognized by **cytotoxic T cells** and specific for human tumors, comprises improved selection of genes encoding target antigens.
DERWENT CLASS: B04 D16
INVENTOR(S): ZAUDERER, M
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002018785	A1	20020214	(200229)*		54

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002018785	A1 Div ex	US 1997-935377	19970922
		US 2001-822250	20010402

PRIORITY APPLN. INFO: US 1997-935377 19970922; US 2001-822250 20010402
AN 2002-239252 [29] WPIDS
AB US2002018785 A UPAB: 20020508
NOVELTY - Identifying (M) a target epitope (I), comprising **screening** products of an expression library generated from DNA/RNA of a cell (C1) expressing (I) with **cytotoxic T cells** (C2) generated against C1 to identify DNA clones expressing (I), or providing C2 specific for a gene product differentially expressed by C1 and measuring cross-reactivity of C2 for C1 in which (I) is identified as a gene product inducing C2, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a viral vector (II) containing a DNA insert flanked by unique sites for restriction enzymes positioned so that religation of the viral vector arms is prevented and the orientation of the insert DNA is fixed and the DNA insert is operatively associated with a strong regulatory element.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine. No supporting data given.

USE - (M) is useful for identifying a target epitope or antigen specific for a tumor cell (claimed). (I) is also useful for identifying target antigens in other target cells against which it is desirable to induce cell-mediated immunity. The antigen identified by (M) is useful in vaccine preparations. (II) is useful for **treating** tumor-bearing mammals, including humans to generate immune response against the tumor cells. (II) is also useful for immunizing or vaccinating tumor-free subjects to prevent tumor formation.

ADVANTAGE - The method can identify potential antigens that are

expressed not only by the pathogen, but also by the host cell whose gene expression is altered as a result of **infection**. Since many pathogens elude immune surveillance by frequent reproduction and mutation, the method is of considerable value to develop a vaccine that targets host gene products that are not likely to be subject to mutation.

DESCRIPTION OF DRAWING(S) - The figure shows the schematic of polymerase chain reaction SELECT method of Representational Difference Analysis.

Dwg.3/14

L12 ANSWER 7 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2002:703674 SCISEARCH
THE GENUINE ARTICLE: 584JH
TITLE: Safety of allogeneic Epstein-Barr virus (EBV)-specific **cytotoxic T lymphocytes** for patients with refractory EBV-related lymphoma
AUTHOR: Sun Q; Burton R; Reddy V; Lucas K G (Reprint)
CORPORATE SOURCE: Univ Alabama, Dept Med, 1900 Univ Blvd, THT 513C, Birmingham, AL 35294 USA (Reprint); Univ Alabama, Dept Med, Birmingham, AL 35294 USA; Univ Alabama, Dept Pediat, Birmingham, AL 35294 USA; Univ Alabama, Dept Pathol, Birmingham, AL 35294 USA
COUNTRY OF AUTHOR: USA
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (SEP 2002) Vol. 118, No. 3, pp. 799-808.
Publisher: BLACKWELL PUBLISHING LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0007-1048.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 46

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Epstein-Barr virus (EBV) causes lymphomas in immunocompromised individuals such as recipients of stem cell or organ transplants and patients with **acquired** immunodeficiency **syndrome** (**AIDS**). EBV has also been **detected** in the Reed-Sternberg cells of approximately 50% of all cases of Hodgkin's disease (HD). The purpose of this study was to examine the safety, and the clinical and immunological effects of infusing allogeneic EBV-specific **cytotoxic T lymphocytes** (**CTL**) for patients with refractory EBV-positive malignancies. In this pilot study, we have **treated** four patients with EBV-related lymphoma using allogeneic EBV-specific **CTL**. Two patients received EBV-specific **CTL** derived from partially human leucocyte antigen (HLA)-matched donors and the other two from HLA-matched siblings. No complications were observed as a result of the **CTL** infusions and all patients showed increased levels of EBV-specific **CTL** precursors (CTLp) post infusion. Of the two organ transplant patients, one had refractory disease and has sustained a complete remission following the T-cell infusions. The second has also been disease free since T-cell infusions, although the efficacy cannot be definitively attributed to **CTL therapy** because this patient received local radiation **therapy** prior to immunotherapy. A patient with **AIDS**-related, EBV-positive lymphoma had disease progression following **CTL** infusions. One HD

patient received HLA 4/6 matched T cells from an unrelated donor and showed a decrease in the size of affected lymph nodes and resolution of B-symptoms post infusion. In conclusion, adoptive immunotherapy with allogeneic EBV-specific **CTL** is safe and mayhave efficacy in patients with high-risk or refractory EBV-related tumours.

L12 ANSWER 8 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:144847 BIOSIS
DOCUMENT NUMBER: PREV200200144847
TITLE: Aggressive Epstein-Barr virus-associated, CD8+, CD30+, CD56+, surface CD3-, natural killer (NK)-like **cytotoxic T-cell** lymphoma.
AUTHOR(S): Tao, Jianguo; Shelat, Suresh G.; Jaffe, Elaine S.; Bagg, Adam (1)
CORPORATE SOURCE: (1) Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, 3400 Spruce St., 7.103 Founders Pavilion, Philadelphia, PA, 19104: adambagg@mail.med.upenn.edu USA
SOURCE: American Journal of Surgical Pathology, (January, 2002) Vol. 26, No. 1, pp. 111-118. http://www.ajsp.com. print. ISSN: 0147-5185.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We report an unusual case of aggressive natural killer (NK)-like **cytotoxic T-cell** lymphoma in a previously healthy immunocompetent West African male. We presented with a fever of unknown origin, subsequently developed erythematous skin nodules, generalized lymphadenopathy, and hepatosplenomegaly, and then died of multiple organ failure. A skin nodule and lymph node biopsy showed an infiltrate of pleomorphic atypical medium and large lymphoid cells with extensive necrosis and prominent apoptosis. Peripheral blood and ascites also harbored these cells, with cytology revealing irregular nuclear folding and basophilic cytoplasm, and some with azurophilic cytoplasmic granules. Flow cytometry and immunohistochemistry demonstrated the expression of CD2, CD7, CD8, CD30, CD56, and cytoplasmic but not surface CD3. In situ **hybridization** demonstrated Epstein-Barr virus transcripts. A monoclonal T-cell receptor gamma chain gene rearrangement was **detected** by polymerase chain reaction. This is the first reported case of an NK-like T-cell lymphoma with these unusual features, making precise classification difficult. Some features suggest an NK1.1 or NKT lymphocyte origin. Because the earliest clinical manifestation was splenomegaly and abnormal liver function, the normal cellular counterpart may be a distinct subset of NK1.1 cells normally present in hepatosplenic sinusoids. This tumor disseminated early and pursued a fulminant clinical course, thus emphasizing the importance of early recognition and diagnosis.

L12 ANSWER 9 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002129828 EMBASE
TITLE: The editor's page.
AUTHOR: Young L.
SOURCE: Epstein-Barr Virus Report, (2002) 9/1 (35-36). ISSN: 0969-9252 CODEN: EVRPBI
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English

L12 ANSWER 10 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-122061 [16] WPIDS
DOC. NO. NON-CPI: N2002-091568
DOC. NO. CPI: C2002-037377
TITLE: **Screening** assays for identifying compounds useful for **treating** immune disorders, comprises identification of compounds that modulate alpha 2-macroglobulin receptor-heat shock protein interaction.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): SRIVASTAVA, P K
PATENT ASSIGNEE(S): (UYCO-N) UNIV CONNECTICUT HEALTH CENT
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001092474	A1	20011206	(200216)*	EN	236
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU CA JP					
AU 2001075205	A	20011211	(200225)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001092474	A1	WO 2001-US18041	20010604
AU 2001075205	A	AU 2001-75205	20010604

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001075205	A Based on	WO 200192474

PRIORITY APPLN. INFO: US 2000-750972 20001228; US 2000-209095P 20000602; US 2000-625137 20000725; US 2000-668724 20000922

AN 2002-122061 [16] WPIDS

AB WO 200192474 A UPAB: 20020308
NOVELTY - **Screening** assays (M1) comprising identification of compounds that modulate alpha 2-macroglobulin (alpha 2M) receptor (which also functions as heat shock protein (HSP) receptor)-HSP interaction, is new.
DETAILED DESCRIPTION - M1 comprises:
(a) identifying (I) a compound that modulates an HSP- alpha 2M receptor-mediated process, by contacting a test compound with HSP and alpha 2M receptor or alpha 2M receptor-expressing cell, and measuring the level of alpha 2M receptor activity or expression, such that if the level of activity or expression measured in the presence of the compound differs from the level of alpha 2M receptor

activity in the absence of the test compound, then a compound that modulates an HSP- alpha 2M receptor-mediated process is identified;

(b) identifying (II) a compound that modulates the binding of HSP to alpha 2M receptor, by contacting HSP with alpha 2M receptor, its fragment, analog, derivative or mimetic, in the present of a test compound and measuring the amount of HSP bound to alpha 2M receptor, its fragment, analog, derivative or mimetic, such that if the amount of bound HSP measured in the presence of the test compound differs from the amount of bound HSP measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the alpha 2M receptor is identified;

(c) identifying (III) a compound that modulates HSP-mediated antigen presentation by alpha 2M receptor-expressing cells, by adding a test compound to a mixture of alpha 2M receptor expressing cells and a complex consisting essentially of HSP non-covalently associated with an antigenic molecule, under conditions conducive to alpha 2M receptor-mediated endocytosis, measuring the level of stimulation of antigen-specific **cytotoxic T cells** by alpha 2M receptor-expressing cells, such that if the level measured in the presence of the test compound differs from the level of the stimulation in the absence of the test compound, then a compound that modulates HSP-mediated antigen presentation by alpha 2M receptor-expressing cells is identified;or

(d) **detecting** (IV) a HSP- alpha 2M receptor-related disorder in a mammal, by measuring the level of activity from an HSP- alpha 2M receptor-mediated process in a patient sample, such that if the measured level differs from the level found in clinically normal individuals, then a HSP- alpha 2M receptor-related disorder is **detected.**

INDEPENDENT CLAIMS are also included for the following:

(1) modulating (M2) an immune response, by administering to a mammal a purified compound that modulates the interaction of HSP with alpha 2M receptor;

(2) **treating** (M3) an autoimmune disorder, by administering to a mammal in need of such **treatment** a purified compound that interferes with the interaction of HSP with the alpha 2M receptor;

(3) **treating** an autoimmune disorder, by administering to a mammal in need of such **treatment,** a recombinant cell that expresses an alpha 2M receptor which decreases the uptake of HSP by a functional alpha 2M receptor;

(4) increasing the immunopotency of a cancer cell or an infected cell;

(5) increasing the immunopotency of a cancer cell or an infected cell, by transforming the cell with a nucleic acid comprising a nucleotide sequence that is operably linked to a promoter, and encodes an alpha 2M receptor polypeptide, and administering the cell to individual in need of **treatment,** so as to obtain an elevated immune response;

(6) a recombinant cancer cell or recombinant infected cell (V) transformed with (N);

(7) a kit (K1);

(8) a kit (K2), in one or more containers;

(9) identifying an alpha 2M receptor fragment capable of binding HSP, by contacting HSP or its peptide-binding fragment with one or more alpha 2M receptor fragments, and identifying an alpha 2M receptor fragment which specifically binds to HSP or its peptide-binding fragment;

(10) identifying (M4) an alpha 2M receptor fragment capable of inducing an HSP- alpha 2M receptor-mediated process, by contacting HSP with a cell expressing alpha 2M receptor fragment and measuring the level of alpha 2M receptor activity in the cell, such that if the level of HSP- alpha 2M receptor-mediated process or activity measured is greater than the level of alpha 2M receptor activity in the absence of the alpha 2M receptor fragment, then an alpha 2M receptor fragment capable of inducing an HSP- alpha 2M receptor-mediated process is identified;

(11) identifying HSP fragment capable of binding an alpha 2M receptor, by contacting an alpha 2M receptor with one or more HSP fragments and identifying HSP fragment which specifically binds to the alpha 2M receptor;

(12) identifying (M5) HSP fragment capable of inducing an HSP-alpha 2M receptor-mediated process;

(13) identifying (M6) a molecule that binds specifically to an alpha 2M receptor;

(14) **screening** for molecules that specifically bind to an alpha 2M receptor;

(15) identifying a compound that modulates the binding of an alpha 2M receptor ligand to the alpha 2M;

(16) identifying a compound that modulates the interaction between the alpha 2M receptor and an alpha 2M receptor ligand;

(17) identifying (M7) a compound that modulates antigen presentation by alpha 2M receptor-expressing cells;

(18) modulating an immune response, by administering to a mammal a purified compound that binds to the alpha 2M receptor;

(19) **treating** or preventing a disease or disorder, by administering to a mammal a purified compound that binds to the alpha 2M receptor;

(20) **treating** an autoimmune disorder, by administering to a mammal in need of such **treatment** a purified compound that binds to the alpha 2M receptor;

(21) stimulating (M8) an immune response in a patient, by administering to the patient blood which has been withdrawn from the patient and **treated** to remove an alpha 2M receptor ligand;

(22) stimulating (M9) an immune response in a patient, by removing alpha 2M receptor ligand from blood withdrawn from the patient, and returning at least a portion of the alpha 2M receptor ligand-depleted blood to the patient;

(23) stimulating (M10) an immune response in a patient, by withdrawing blood from the patient, removing alpha 2M receptor ligand from the blood and returning at least a portion of alpha 2M receptor ligand-depleted blood to the patient; and

(24) a kit (K3);

ACTIVITY - Immunosuppressive; antiinflammatory; cytostatic; virucide; antilipemic; nootropic; antidiabetic; osteopathic.

MECHANISM OF ACTION - Modulator of interaction between alpha 2M receptor and HSP (claimed). No supporting data given.

USE - The interaction between alpha 2M receptor and HSP is useful in screening assays for identifying compounds that modulate the interaction of alpha 2M receptor and HSP. The identified compounds are useful for treating an autoimmune disorder, disease or disorder involving disruption of antigen presentation or endocytosis or cytokine clearance or inflammation, proliferative disorder, viral disorder or other infectious diseases, hypercholesterolemia, Alzheimer's disease, diabetes or osteoporosis (claimed).

Dwg.0/14

L12 ANSWER 11 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-082990 [11] WPIDS
DOC. NO. CPI: C2002-025139
TITLE: New composition, useful for **treatment** and/or prophylaxis of cancer and tumor, comprises immunostimulatory molecule and animal cells cultured in presence of interferon to enhance antigen presenting function of the cells.
DERWENT CLASS: B04 D16
INVENTOR(S): RALPH, S J
PATENT ASSIGNEE(S): (MONU) UNIV MONASH
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001088097	A1	20011122	(200211)*	EN	127
AU 2001058040	A	20011126	(200222)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001088097	A1	WO 2001-AU565	20010517
AU 2001058040	A	AU 2001-58040	20010517

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001058040	A	Based on	WO 200188097

PRIORITY APPLN. INFO: AU 2000-7553 20000517
AN 2002-082990 [11] WPIDS
AB WO 200188097 A UPAB: 20020215
NOVELTY - A composition of matter (I) comprising an immunostimulatory molecule and animal cells cultured in the presence of at least one interferon (IFN) for a time and under conditions sufficient to enhance the antigen presenting function of the cells, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) enhancing (M1) immunopotentiation of animal cells comprising:

(a) culturing animal cells expressing an immunostimulatory membrane molecule in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the cells; or

(b) culturing animal cells in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen

presenting functions of the cells, and combining the cells so cultured with an immunostimulatory molecule in soluble form;

(2) enhancing (M2) or otherwise improving the **immunogenicity** of an antigen comprising providing animal cells cultured in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the cells and loading the antigen onto the IFN-**treated** animal cells;

(3) a composition of matter (II) for eliciting an immune response against a target antigen, comprises animal cells cultured in the presence of at least one IFN for a time under conditions sufficient to enhance the antigen presenting functions of the cells, where an antigen corresponding to target antigens has been loaded onto IFN-**treated** animal cells;

(4) a vaccine (III) for stimulating a host's immune system, comprises (I) or (II);

(5) a kit (IV) comprising (I);

(6) assessing (M3) the responsiveness of animal cells to **treatment** with at least one IFN comprising **detecting** in the animal cells the level and/or functional activity of a polypeptide involved in interferon signaling, a modulatory agent that modulates the polypeptide, or a downstream cellular target of the polypeptide, or the level of an expression product of a genetic sequence encoding the polypeptide, the modulatory agent or the downstream cellular target;

(7) use of a target cell (V) in an assay for **detecting** cytolytic activity of a **cytotoxic T lymphocyte** (**CTL**) for the target cell, where the target cell has been cultured in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting function of the cell;

(8) **detecting** (M4) **CTL** mediated lysis of a target cell comprising providing a target cell in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the target cells, contacting the target cell with a **CTL** that has cytolytic activity for the target cell and **detecting** **CTL**-mediated lysis of the target cell; and

(9) use of an antigen binding molecule that is immuno-interactive with a polypeptide or modulatory agent, or a **detector** polynucleotide or oligonucleotide that **hybridizes** to the expression product in a kit for assessing the responsiveness of animal cells to **treatment** with at least one IFN.

ACTIVITY - Cytostatic; antitumor; antibacterial; virucide; fungicide; protozoacide.

MECHANISM OF ACTION - Vaccine; enhancer of antigen presenting function of cells (claimed). Preclinical trials were conducted using immunopotentiating composition as a cancer vaccine. **Treatment** of cells with gamma interferon (IFN) for 72 hours and beta -IFN for 48 hours was shown to optimally induce increased levels of surface expression of major histocompatibility complex (MHC) class I on melanoma cells, particularly on human melanoma cells. Levels of intracellular adhesion molecule (ICAM)-1 and B7 antigens on the human cells were also elevated by IFN **treatment**. However, given the common loss of B7 expression on these cells, the immunopotentiating composition included transfection to express B7-1 antigen. The transfected B7 expressing

murine melanoma cells were shown to be unaltered in their responses to the optimal IFN **treatment** showing similar strong inductions of MHC class I antigen. Results from studies with the B16 melanoma model showed that the expression of B7-1 and IFN **treatment** were important for producing CD8 positive **cytotoxic T lymphocytes** (**CTLs**) with potent cytolytic activity against B16 cancer cells and that these cells were capable of lysing target cells even though they did not express B7 antigen. Given the level of immunity shown to be induced by the B7Hi interferon **treated** B16 cells measured by cytotoxicity assay, the same cell preparations were tested for their ability to induce anti-cancer immunity in whole animals when injected as a vaccine. The protocol compared the use of B7Hi/B16 transfected cells to vaccination with wild type B16 cells. The cells were irradiated and cohorts of mice were vaccinated by intraperitoneal injection weekly for up to six weeks. Vaccinated mice were challenged at week 7 with an injection subcutaneously on the rear flank with 5 multiply 10 to the power of 5 B7Med B16 cells. The results showed that all twenty control animals receiving only the challenge cancer cells succumbed to a 2 cm tumor growth by day 38. However, mice vaccinated with the B7Hi interferon **treated** immunopotentiating composition produced the greatest resistance to the challenge with 90% surviving with no sign of tumor and continued to remain tumor free thereafter. Thus, it was concluded that the B7Hi/IFN **treated** immunopotentiating composition induced potent CD8 positive **CTL** responses and were capable of providing sufficient immunity to protect the majority of vaccinated mice from the cancer cells.

USE - (I) or (III) is useful for **treatment** and/or prophylaxis of a disease or condition, such as tumorigenesis, by administering (I) or (III) to the patient. (I) which comprises the soluble immunostimulatory molecule and the cultured animal cells is administered separately, sequentially or simultaneously to the patient (claimed). (I) or (V) is useful for **treatment** and/or prophylaxis of cancer. (I), (II) or (V) is useful for **treating** viral, bacterial, fungal and protozoal **infections**.

Dwg.0/15

L12 ANSWER 12 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 2001:585359 SCISEARCH

THE GENUINE ARTICLE: 452QR

TITLE: Transcription pattern of human herpesvirus 8 open reading frame K3 in primary effusion lymphoma and Kaposi's sarcoma

AUTHOR: Rimessi P; Bonaccorsi A; Sturzl M; Fabris M; Brocca-Cofano E; Caputo A; Melucci-Vigo G; Falchi M; Cafaro A; Cassai E; Ensoli B (Reprint); Monini P

CORPORATE SOURCE: Ist Super Sanita, Virol Lab, Viale Regina Elena 299, I-00161 Rome, Italy (Reprint); Ist Super Sanita, Virol Lab, I-00161 Rome, Italy; Univ Ferrara, Microbiol Sect, Dept Diagnost & Expt Med, I-44100 Ferrara, Italy; Ist Super Sanita, Ultrastrutture Lab, I-00161 Rome, Italy; GSF, Inst Mol Virol, Natl Res Ctr Environm & Hlth, D-85764 Neuherberg, Germany

COUNTRY OF AUTHOR: Italy; Germany

SOURCE: JOURNAL OF VIROLOGY, (AUG 2001) Vol. 75, No. 15, pp. 7161-7174.

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0022-538X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 74

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human herpesvirus 8 (HHV-8) is found in immunoblastic B cells of patients with multicentric Castleman's disease (MCD) and, predominantly in a latent form, in primary effusion lymphoma (PEL) cells and Kaposi's sarcoma (KS) spindle cells. Recent studies have shown that upon reactivation, HHV-8 expresses factors that downregulate major histocompatibility class I proteins and coactivation molecules and that may enable productively infected cells to escape **cytotoxic T lymphocytes** and natural killer cell responses. One of these viral factors is encoded by open reading frame (ORF) K3. Here we show that in PEL cells, ORF K3 is expressed through viral transcripts that are induced very early upon virus reactivation, including bicistronic RNA molecules containing coding sequences from viral ORFs K3 and 70. Specifically, we found that a bicistronic transcript was expressed in the absence of de novo protein synthesis, thereby identifying a novel HHV-8 immediate-early gene product. Several features of the RNA molecules encoding the K3 product, including multiple transcriptional start sites, multiple donor splicing sites, and potential alternative ATG usage, suggest that there exists a finely tuned modulation of ORF K3 expression. By contrast, ORF K3 transcripts are not **detected** in the majority of cells present in KS lesions that are latently infected by the virus, suggesting that there are other, as-yet-unknown mechanisms of immune evasion for infected KS spindle cells, Nevertheless, because HHV-8 viremia precedes the development of KS lesions and is associated with the recrudescence of MCD symptoms, the prompt expression of ORF K3 in productively infected circulating cells may be important for virus pathogenesis. Thus, molecules targeting host or viral factors that activate ORF K3 expression or inactivate the biological functions of the K3 product should be exploited for the prevention or **treatment** of HHV-8-associated diseases in at-risk individuals.

L12 ANSWER 13 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001345987 EMBASE
TITLE: Editorial comment on **detection** of Epstein-Barr virus DNA in peripheral blood of paediatric patients with Hodgkin's disease by real-time polymerase chain reaction by Wagner and colleagues.
AUTHOR: Magrath I.
CORPORATE SOURCE: I. Magrath, Intl. Network for Can. Treat./Res., Brussels, Belgium. imagrath@inctr.be
SOURCE: European Journal of Cancer, (2001) 37/15 (1812-1815). Refs: 30
ISSN: 0959-8049 CODEN: EJCAEL
PUBLISHER IDENT.: S 0959-8049(01)00221-0
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 004 Microbiology
016 Cancer

037 Drug Literature Index
LANGUAGE: English

L12 ANSWER 14 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:459852 SCISEARCH
THE GENUINE ARTICLE: 437LL
TITLE: Rapid and wide-reaching delivery of **HIV**-1 env DNA vaccine by intranasal administration
AUTHOR: Tadokoro K; Koizumi Y; Miyagi Y; Kojima Y; Kawamoto S; Hamajima K; Okuda K (Reprint); Tanaka S; Onari K; Wahren B; Aoki I; Okuda K
CORPORATE SOURCE: Yokohama City Univ, Sch Med, Dept Bacteriol, Kanazawa Ku, 3-9 Fukuura, Yokohama, Kanagawa 2360004, Japan (Reprint); Yokohama City Univ, Sch Med, Dept Bacteriol, Kanazawa Ku, Yokohama, Kanagawa 2360004, Japan; Yokohama City Univ, Sch Med, Dept Internal Med, Yokohama, Kanagawa 2360004, Japan; Yokohama City Univ, Sch Med, Dept Pathol, Yokohama, Kanagawa 2360004, Japan; Tokyo Dent Coll, Dept Bacteriol, Mihama Ku, Masago, Japan; Yokohama Minami Kyosai Hosp, Dept Orthoped Surg, Yokohama, Kanagawa, Japan; Karolinska Inst, Swedish Inst Infect Dis Control, Stockholm, Sweden
COUNTRY OF AUTHOR: Japan; Sweden
SOURCE: VIRAL IMMUNOLOGY, (5 MAY 2001) Vol. 14, No. 2, pp. 159-167.
Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538 USA.
ISSN: 0882-8245.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 41
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although the potential of DNA vaccination is now beginning to be greatly appreciated, no detailed study of its localization in tissue or its expression kinetics has been reported. In this study, we investigated these issues using **HIV**-1 DNA plasmids administered either intranasally or intramuscularly, Fluorescence in situ **hybridization** (FISH) revealed that the **human** immunodeficiency **virus** (**HIV**) plasmids administered intranasally localized in the alveoli, lung, liver, spleen, regional lymph nodes, kidney, fetus, and esophagus, These **HIV** plasmids were **detected** 2 to 4 weeks after administration. We **detected** messenger RNA production of **HIV** env gene in the lung, liver and spleen, and **human** immunodeficiency **virus** type 1 (**HIV** -1)-specific proteins were **detectable** in the lung, These observations may provide important information for understanding the mechanisms of strong immune activation induced by DNA vaccination via the intranasal route. This technology of DNA administration suggests possible practical applications for vaccination and probably for gene **therapy**.

L12 ANSWER 15 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:485292 BIOSIS
DOCUMENT NUMBER: PREV200100485292
TITLE: Neuroimmunobiology of head/neck cancer.
AUTHOR(S): Cajulis, E. (1); Romeo, H.; Fiala, M.; Chiappelli, F.

(1)
CORPORATE SOURCE: (1) Oral Biology and Medicine, UCLA, Los Angeles, CA USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 23. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Head/neck cancers, excluding brain cancer, account for over 30,000 cases/y in the U.S., with >30% mortality and <55% 5-year survival, with little change in the past 30 yrs. They afflict most often subjects older than 45 yrs of age, which is significant in light of the projected rise in the aging population in the next decades. We have shown involvement of **CTL** migration and maturation in the surveillance of tongue squamous cell carcinoma (SCC). We have established the role of the superior cervical ganglion in modulating surveillance of breast metastases to the head/neck region, and the role of the glossopharyngeal nerve (cranial nerve IX) in mediating neuroimmunity in the oral cavity. These data support the role of the nervous system in regulating recruitment of immune cells at sites of **infection** and cancers. Ongoing studies confirm this hypothesis and indicate differential migration of T cells to proliferating (CD3+CD40L-) vs. necrotic (CD3+CD40L+) gliomas, the most common brain cancer. Tumor neuroimmune surveillance depends upon the recognition of certain tumor specific genes. By **microarray**, we have revealed the modulated expression of several genes (e.g., TRAIL) uniquely expressed by the tongue SCC lines tested. These data indicate that the identification of epitopes unique to certain head/neck cancers is possible. Ongoing parallel experiments are aimed at defining the expression of tumor specific genes in prostate carcinomas, because of their significant potential, together with breast carcinomas, to establish metastases to the axial, cranial and facial skeletons. Further characterization of the neuroimmunobiology of head/neck tumors should lead to improved **detection**, diagnostic and **treatment**.

L12 ANSWER 16 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-376533 [32] WPIDS
DOC. NO. NON-CPI: N2000-282704
DOC. NO. CPI: C2000-113935
TITLE: Novel method of identifying target epitopes or antigens specific for human tumors, cancers and infected cells involving **screening** expression library products of a cell expressing the target epitope.
DERWENT CLASS: B04 D16 P14
INVENTOR(S): ZAUDERER, M
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000028016	A1	20000518	(200032)*	EN	132

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT UA UG UZ VN YU ZW
AU 9913977 A 20000529 (200041)
EP 1137769 A1 20011004 (200158) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002529082 W 20020910 (200274) 144

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000028016	A1	WO 1998-US24029	19981110
AU 9913977	A	WO 1998-US24029	19981110
		AU 1999-13977	19981110
EP 1137769	A1	EP 1998-957808	19981110
		WO 1998-US24029	19981110
JP 2002529082	W	WO 1998-US24029	19981110
		JP 2000-581183	19981110

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9913977	A	Based on	WO 200028016
EP 1137769	A1	Based on	WO 200028016
JP 2002529082	W	Based on	WO 200028016

PRIORITY APPLN. INFO: WO 1998-US24029 19981110
AN 2000-376533 [32] WPIDS
AB WO 200028016 A UPAB: 20000706
NOVELTY - Identifying (I) a target epitope (TE) comprising **screening** the products of an expression library from a cell (C) expressing TE, with **cytotoxic T cells** (**CTLs**) generated against the C to identify DNA clones expressing TE, or providing a **CTL** specific for a gene product (GP) differentially expressed by a C and measuring the cross-reactivity of the **CTL**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a viral vector (V) containing a DNA insert operably linked to a strong regulatory element and flanked by unique sites for restriction enzymes positioned so that religation of viral vectors arms is prevented and orientation of insert DNA is fixed;

(2) a transgenic animal (II) tolerized with a non-tumorigenic cell line that does not express co-stimulator activity; and

(3) a **CTL** derived from (II).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine.

Groups of 5 mice of the BALB/c strain syngeneic to the murine tumors were immunized with vaccinia virus recombinant for a full length cDNA differentially expressed in all four murine tumor lines but not the parental B/c.N cells. Each group of mice was assayed for induction of protective immunity by challenge with a tumorigenic inoculum of 1 multiply 106 BCA 39 tumor cells. Results not given.

USE - (I) is useful for identifying tumor specific target epitopes (TEs) (claimed) and antigens which are useful in **immunogenic** compositions or vaccines to induce the regression of tumors, cancers or **infections** in mammals including human. The genes expressed in a panel of tumor cells that are derived from single immortalized, non-tumorigenic cell line are used to generate HLA restricted **CTLs** which are evaluated for activity against tumor cells.

ADVANTAGE - (I) is useful for identifying target antigens in other target cells against which it is desirable to induce cell mediated immunity. The method is useful to identify potential antigens expressed not only by the pathogen but also by the host cells whose gene expression is altered as a result of **infection**. The differential gene expression strategies can be applied to identify **immunogenic** molecules of cells infected with virus, fungus or mycobacterium.

DESCRIPTION OF DRAWING(S) - The diagram shows a schematic of the PCR Select (RTM) method of Representational Difference Analysis.
Dwg.3/14

L12 ANSWER 17 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-160677 [14] WPIDS
CROSS REFERENCE: 2000-160676 [14]
DOC. NO. NON-CPI: N2000-119889
DOC. NO. CPI: C2000-050164
TITLE: New GP, NP, VP24, VP30, VP35 and VP40 Ebola virus proteins, useful for prevention, **treatment** or diagnosis of Ebola **infection**, particularly where expressed from virus replicons.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HART, M K; PUSHKO, P; SCHMALJOHN, A L; SMITH, J F; WILSON, J A
PATENT ASSIGNEE(S): (USME-N) US MEDICAL RES INST INFECTIOUS DISEASES; (HART-I) HART M K; (PUSH-I) PUSHKO P; (SCHM-I) SCHMALJOHN A L; (SMIT-I) SMITH J F; (WILS-I) WILSON J A
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000000617	A2	20000106	(200014)*	EN	70
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9950844	A	20000117	(200026)		
EP 1119627	A2	20010801	(200144)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 2002164582	A1	20021107	(200275)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000000617	A2	WO 1999-US14311	19990622

AU 9950844	A	AU 1999-50844	19990622
EP 1119627	A2	EP 1999-935350	19990622
		WO 1999-US14311	19990622
US 2002164582	A1 Provisional	US 1998-91403P	19980629
		US 1999-337946	19990622

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9950844	A	Based on	WO 200000617
EP 1119627	A2	Based on	WO 200000617

PRIORITY APPLN. INFO: US 1998-91403P 19980629; US 1999-337946 19990622

AN 2000-160677 [14] WPIDS

CR 2000-160676 [14]

AB WO 200000617 A UPAB: 20021120

NOVELTY - GP, NP, VP24, VP30, VP35 and VP40 Ebola virus proteins (or their immunologically identifiable portions) comprising sequences (I)-(VII) (where VP30 can be encoded by sequences (IV) and/or (V)) of 251-739 amino acids (aa), are new (all sequences are fully defined in the specification).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) DNA sequences (VIII)-(XIV) of 847-2428 nucleotides (nt), or their fragments of at least 15 nt and/or which encode at least 5 aa of sequences (I)-(VII), encoding a GP, NP, VP24, VP30, VP35 or VP40 Ebola virus protein (where VP30 can be encoded by (XI) and/or (XIV));

(2) a recombinant DNA construct (A) containing, in a vector, at least one of sequences (VIII)-(XIV) or their fragments of at least 15 nt;

(3) self-replicating RNA (B) produced by any one of EboVP24ReP, EboVP30ReP, EboVP35ReP, EboVP40ReP, EboVPNPReP, EboVPGPReP or EboVP30ReP (constructs of (A));

(4) **infectious** alphavirus particles (C) produced by packaging (B);

(5) prokaryotic/eukaryotic host cells (D) transformed with (A);

(6) production of Ebola virus proteins by culturing (D);

(7) antibodies (Ab) (E) raised against peptides of sequences (I)-(VII) and sequences of 11 and 23 amino acids (XV)-(XVI) respectively;

(8) **detecting** Ebola virus **infection** by formation of immune complex with (E);

(9) **detecting** Ebola GP RNA by polymerase chain reaction (PCR), using primers derived from (VIII);

(10) a diagnostic kit (F) for Ebola **infection** comprising fragments of at least 12 consecutive nt from (VIII) specific for the amplification of DNA or RNA of Ebola virus by PCR amplification plus ancillary reagents for **detection**; and

(11) a vaccine comprising (C);

All sequences are fully defined in the specification

ACTIVITY - Antiviral.

Capped replicon RNAs, from Ebola protein VP24, were produced by in vitro T7 run-off transcription of linearized plasmids and used, together with two helper RNAs expressing the structural proteins of Venezuelan equine encephalitis (VEE) virus, to transfect baby

hamster kidney cells. Recombinant VEE virus replicons were recovered from the culture supernatant by centrifugation through a 20% sucrose solution. Balb/c mice were injected twice with 2 million focus-forming units of the resulting replicons (designated EboVP24VRP), then 1 month after the second injection challenged with 105 plaque-forming units of mouse-adated Ebola virus. All animals survived the challenge, compared with none of unvaccinated controls. Another example shows that immune serum from animals vaccinated with a replicon based on the GP protein (but not those based on other Ebola proteins) passively protected unvaccinated mice against challenge.

MECHANISM OF ACTION - Vaccine.

USE - (A) are useful to produce the following:

(1) the Ebola virus proteins as described above;

(2) self-replicating RNA; or

(3) **infectious** alphavirus particles;

all of which (also the constructs themselves) are useful in pharmaceutical compositions and protective vaccines. The Ebola proteins are also useful for the diagnosis of Ebola **infection** (by **detecting** antibodies) and for raising specific antibodies (E), which can be used to **detect** the proteins. DNA sequences (VIII)-(XIV) are useful as probes and primers for diagnostic **hybridization** or polymerase chain reaction assays for **detecting** Ebola virus (all claimed).

Dwg.0/4

L12 ANSWER 18 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-571181 [53] WPIDS
DOC. NO. CPI: C2000-170161
TITLE: Recombinant chimeric nucleic acids encoding retroviral gag-fusion partner fusion proteins for producing pseudovirions which are useful as vaccines for **treating** and preventing cancer and **acquired** immunodeficiency **syndrome** (**AIDS**).
DERWENT CLASS: B04
INVENTOR(S): GONDA, M A; TOBIN, G J
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6099847	A	20000808	(200053)*		29

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6099847	A	Provisional	US 1996-20463P	19960516
			US 1997-857385	19970515

PRIORITY APPLN. INFO: US 1996-20463P 19960516; US 1997-857385 19970515
AN 2000-571181 [53] WPIDS
AB US 6099847 A UPAB: 20001023
NOVELTY - A recombinant chimeric nucleic acid (I) comprising a

retroviral gag sequence, a target nucleic acid sequence derived from a nucleic acid encoding a fusion partner selected from Env, an interleukin (IL), tumor necrosis factor (TNF), granulocyte macrophage stem cell factor (GM/SCF), a non-retroviral viral antigen and a cancer antigen and a frame-shift (fs) site, is new.

DETAILED DESCRIPTION - A recombinant chimeric nucleic acid (I) comprising a retroviral gag sequence, a target nucleic acid sequence derived from a nucleic acid encoding a fusion partner selected from Env, an interleukin (IL), tumor necrosis factor (TNF), granulocyte macrophage stem cell factor (GM/SCF), a non-retroviral viral antigen and a cancer antigen and a frame-shift (fs) site, is new. In (I) the gag and target sequences are transcribed from a single start site of transcription and are in different reading frames.

INDEPENDENT CLAIMS are also included for the following:

(1) a pseudovirion (II) comprising a retroviral gag protein and a fusion partner, where the fusion protein partner is present in a Gag-fs-fusion partner fusion protein;

(2) an **immunogenic** composition (III) comprising (II);

(3) a particulate vaccine (IV) comprising (II);

(4) a fusion protein (V) comprising a retroviral Gag sequence, a translation reading frame switching sequence and a fusion partner; and

(5) a method (VI) of making a pseudovirion comprising expressing a nucleic acid encoding a Gag-fs-fusion partner fusion protein in a cell, where the cell translates the nucleic acid into a protein comprising a Gag sequence and another protein comprising a gag sequence and a fusogenic partner.

ACTIVITY - Cytostatic; Anti-**HIV** (**human** immunodeficiency **virus**).

MECHANISM OF ACTION - Vaccine. The effect of non-**infectious** virus-like particles (VLPs) produced by insect cell expression of the **HIV**-1 Gag precursor protein by recombinant baculovirus in generating an **HIV**-specific **cytotoxic T-lymphocyte** (**CTL**) response was studied. Balb/c mice were inoculated with 2 mu g of Gag or Gag-SU (Gag coding sequence containing gp120) VLPs in phosphate buffered saline (PBS). Three weeks following the inoculation, splenocyte cultures from the mice were pooled, stimulated in vitro and tested for lysis of Gag and Env target cells. Splenocytes from mice immunized with Gag-SU VLPs lyzed both Gag and Env targets.

USE - (II), (III) or (IV) is useful for eliciting a **cytotoxic T-lymphocyte** (**CTL**) response against Env but does not elicit antibodies against Env (claimed). Pseudovirions containing Gag and Env protein sequences are useful for **treating** and preventing virally-mediated diseases such as **AIDS** (**acquired** immune deficiency **syndrome**) and pseudovirions containing cancer protein sequences are useful for **treating** and preventing cancer. They are also useful in assays to **detect** antisera to **HIV** in an individual infected with **HIV**.

Dwg.0/3

L12 ANSWER 19 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:836218 SCISEARCH
THE GENUINE ARTICLE: 369KB
TITLE: **HIV**-1 and its causal relationship to immunosuppression and nervous system disease in **AIDS**: A review

AUTHOR: Sotrel A; DalCanto M C (Reprint)
CORPORATE SOURCE: NORTHWESTERN UNIV, SCH MED, DEPT PATHOL, DIV NEUROPATHOL, 303 E CHICAGO AVE, CHICAGO, IL 60611 (Reprint); NORTHWESTERN UNIV, SCH MED, DEPT PATHOL, DIV NEUROPATHOL, CHICAGO, IL 60611; UNIV ILLINOIS, DEPT PATHOL, CHICAGO, IL
COUNTRY OF AUTHOR: USA
SOURCE: HUMAN PATHOLOGY, (OCT 2000) Vol. 31, No. 10, pp. 1274-1298.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0046-8177.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 423

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Acquired** immune deficiency **syndrome** (**AIDS**), caused by **human** immunodeficiency **virus** type 1 (**HIV**-1), has claimed more than 10 million lives over the past 15 years. There are approximately 30 million **HIV**-positive people worldwide, 89% of whom reside in sub-Saharan Africa and Asia. The intricate relationship between the virus and HN-related human multisystem pathology prompted scientists to modify many previously established concepts about **infectious** diseases and immunology, and to test new ones. The results of this work helped resolve many, albeit not all, long-standing problems concerning **HIV**-1 immune escape, its cellular tropism, and pathogenesis of **HIV**-related immunosuppression and nervous system disease. The most impressive advances have been made in antiretroviral drug **treatment** of **HIV infection**, which has resulted in dramatically reducing **AIDS**-related mortality, morbidity, and perinatal transmission. However, considering the magnitude of the worldwide **HIV-AIDS** pandemic, prohibitive cost and unusually exacting nature of combination drug **treatment**, as well as the emergence of drug-resistant **HIV** mutants, the disease and virus remain formidable and unpredictable, particularly in the area of prevention and vaccine development. Here, we have reviewed the most pertinent recently published studies of various aspects of **HIV/AIDS** intended to answer the following questions: what have we learned and what remains to be **determined** regarding this unorthodox viral disorder? HUM PATHOL 31:1274-1298. Copyright (C) 2000 by W.B. Saunders Company.

L12 ANSWER 20 OF 37 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000391439 MEDLINE
DOCUMENT NUMBER: 20362733 PubMed ID: 10905059
TITLE: **Cytotoxic T-cell** lymphoma diffusely involving the entire gastrointestinal tract associated with Epstein-Barr virus and tubercle bacilli **infection.**
AUTHOR: Abe Y; Muta K; Ohshima K; Hirase N; Matsushima T; Yufu Y; Nishimura J; Nawata H
CORPORATE SOURCE: Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.. abey@intmed3.med.kyushu-

u.ac.jp
SOURCE: INTERNATIONAL JOURNAL OF HEMATOLOGY, (2000 Jun) 71 (4) 379-84.
Journal code: 9111627. ISSN: 0925-5710.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000811

AB We describe a rare case of cytotoxic gastrointestinal T-cell lymphoma with protein-losing enteropathy. Initial examination revealed the coexistence of T-cell lymphoma and tuberculosis in the mesenteric lymph node and liver. Despite anti-tuberculosis and anti-cancer **treatment**, the patient experienced chronic diarrhea and malabsorption and died approximately 3 years after onset. Autopsy specimens revealed medium-sized lymphoma cells, with a phenotype of CD3+, CD4-, CD7+, CD8+, CD30-, CD56-, CD103 (HML-1)-, TIA-1+, and granzyme B+, proliferating primarily and consistently in the mucosa of the entire bowel tract from esophagus to rectum. Interestingly, Epstein-Barr virus (EBV)-encoded small nuclear RNAs were **detected** in the tumors by in situ **hybridization**. Southern blot analysis revealed monoclonal proliferation in the EBV-infected T cells. Although the present case can possibly be categorized as an intestinal T-cell lymphoma according to the Revised European-American Lymphoma Classification, the case showed a unique clinical course and distribution of lymphoma cells. We present here an interesting case of gastrointestinal **cytotoxic T-cell** lymphoma and examine the possible association with **infectious** agents.

L12 ANSWER 21 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000302528 EMBASE
TITLE: Gastrointestinal T cell lymphoma: Predominant cytotoxic phenotypes, including alpha/beta, gamma/delta T cell and natural killer cells.
AUTHOR: Katoh A.; Ohshima K.; Kanda M.; Haraoka S.; Sugihara M.; Suzumiya J.; Kawasaki C.; Shimazaki K.; Ikeda S.; Kikuchi M.
CORPORATE SOURCE: Dr. K. Ohshima, Department of Pathology, School of Medicine, Fukuoka University, Nanakuma 7-45-1, Jonan-ku, Fukuoka 814-01, Japan
SOURCE: Leukemia and Lymphoma, (2000) 39/1-2 (97-111).
Refs: 51
ISSN: 1042-8194 CODEN: LELYEA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Gastrointestinal T cell lymphoma (TCL) is a rare subset of peripheral TCL, presenting with or without cytotoxic phenotype, a history of coeliac disease (CD) and enteropathy. However, CD is rare

in Japan. Here, we describe the clinicopathological features of 18 Japanese cases. Lesions were found in the small intestine (n=13), stomach (n=3) and colon (n=2). Seven patients presented with enteropathy but none had a history of CD. Lymphomas appeared as ulceration (n=11), tumour formation (n=6), or polypoid growth (n=1). Histologically (REAL classification), neoplastic lesions were composed of intestinal type T cell lymphoma (ITCL, n=13, including one case with NK type), anaplastic large cell (ALCL, n=2), adult T cell leukaemia/lymphoma (ATLL, n=2), and lymphoblastic type (n=1). Epstein Barr virus **infection** was **detected** by EBER-1 in situ **hybridization** in 6 of 11 cases with ITCL but not in the other types. ALCL expressed CD30. CD56 was expressed in 3 of 11 cases of ITCL but not in other types. Among the 10 examined cases, 8 were .alpha..beta. T cell type [CD2+, CD3+, T cell receptor (TCR).delta.-1-, .beta.F1+], one was .gamma..delta. T cell type [CD2+, CD3+, TCR.delta.-1+, .beta.F1-], and the remaining case expressed natural killer (NK) cell type [CD2+, CD3-, CD56+, TCR.delta.-1-, .beta.F1-]. Among the 8 examined cases, 3 expressed CD103 molecule, which was associated with extrathymic T cells of intraepithelial lymphocytes. All cases except ATLL expressed the cytotoxicity-associated molecule of TIA-1, and 11 of 14 TIA-1 positive cases expressed activated cytotoxic molecules of perforin, granzyme B, and/or Fas ligand. Despite the morphological, genetic and phenotypic heterogeneity, prognosis was poor, and 11 of 13 patients with small intestinal lesions died albeit appropriate **treatment**, but 3 of 4 patients with gastric or colonic lesions were still alive. The main cause of death was intestinal perforation. The latter might be due to the site specificity of small intestine and tumour cytotoxicity.

L12 ANSWER 22 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:293781 BIOSIS
DOCUMENT NUMBER: PREV200100293781
TITLE: Characterization of autoreactive T-cells in aplastic anemia.
AUTHOR(S): Zeng, Weihua (1); Maciejewski, Jaroslaw P. (1); Young, Neal S. (1)
CORPORATE SOURCE: (1) Hematology Branch, National Heart, Lung, and Blood Institute, Bethesda, MD USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 5a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Despite progress in understanding the pathophysiology of aplastic anemia (AA), the antigens that drive immune-mediated stem cell destruction are not identified. Response to immunosuppression remains the strongest clinical evidence of an immune pathophysiology, bolstered by laboratory demonstration of a proximal Th1 process involving **cytotoxic T cell** activation, gamma-interferon expression, and Fas-mediated apoptosis of CD34 cells. Early events are not well characterized. Inciting antigens could arise from molecular mimicry with **infectious** agents or from proteins modified by drug/chemical interaction; over

or aberrant expression of normal self antigens might also be **immunogenic**. We examined the T-cell receptor (TCR) repertoire of lymphocyte clones derived from a patient with the AA/PNH syndrome; his HLA antigens were A32 A33, B35 B51; DR11, DR15. T cells showed an activated phenotype and displayed marked Vbeta skewing, especially of Vbeta13 and Vbeta5. T-cell lines were established from sorted CD4 and CD8 cells, in which CD69 expression indicated in vivo activation. A total of 105 CD4 and 30 CD8 cell clones were immortalized using herpesvirus saimiri. TCRs of these clones was analyzed using polymerase chain reaction with Vbeta-specific primers. Most (24/30) activated CD4 clones displayed Vbeta5 TCR and the majority (8/12) of CD8 clones expressed Vbeta13. Sequence analysis of the TCR CDR3 region revealed identity for all CD4 Vbeta5 and CD8 Vbeta13 clones, respectively, suggesting that these TCR were over-utilized among activated T-cells. In vitro, T-cell clones carrying the specific TCR were cytotoxic for CD34 cells and inhibited hematopoietic colony formation in vitro for patient target cells, but not for HLA-matched normal marrow targets. A representative CD4 clone showed a Th1 secretion pattern, while a CD8 clone was of the terminal effector phenotype (CD45RO, CD28-, CD57). By specific PCR, we found that the same Vbeta5 spectratype was also present in 11/30 AA patients bearing the DR15 haplotype and 5/7 matched for HLA-B Vbeta13 spectratype. We were unable to **detect** these specific TCR sequences among normal, HLA-matched individuals. As quantitated by Southern **hybridization** of TCR Vbeta PCR products using specific CDR3 probes, the numbers of T-cell displaying these spectratype decreased in 3/4 patients responding to immunosuppressive **therapy**. These striking TCR similarities suggest first, that there is limited heterogeneity in the T cell response in individual patients and, second, that AA patients may recognize similar antigens. Furthermore, these T cell clones should be useful to identify target peptides in expression libraries that activate autoreactive T cells.

L12 ANSWER 23 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-430394 [36] WPIDS
CROSS REFERENCE: 1997-480153 [44]; 1999-590729 [50]; 2002-556723 [59]; 2002-626537 [67]
DOC. NO. NON-CPI: N1999-320416
DOC. NO. CPI: C1999-126860
TITLE: New isolated apoptosis inducing molecule II polypeptides.
DERWENT CLASS: B04 C07 D16 S03
INVENTOR(S): EBNER, R; RUBEN, S M; ULLRICH, S; YU, G
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC; (EBNE-I) EBNER R; (RUBE-I) RUBEN S M; (ULLR-I) ULLRICH S; (YUGG-I) YU G; (ZHAI-I) ZHAI Y; (ZHAN-I) ZHANG
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9935262	A2	19990715	(199936)*	EN	164

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI

SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9921063 A 19990726 (199952)
AU 9929721 A 19990906 (200003)
EP 1044270 A2 20001018 (200053) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002500043 W 20020108 (200206) 237

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9935262	A2	WO 1999-US242	19990107
AU 9921063	A	AU 1999-21063	19990107
AU 9929721	A	AU 1999-29721	19990219
EP 1044270	A2	EP 1999-901341	19990107
		WO 1999-US242	19990107
JP 2002500043	W	WO 1999-US242	19990107
		JP 2000-527646	19990107

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9921063	A	Based on	WO 9935262
AU 9929721	A	Based on	WO 9942584
EP 1044270	A2	Based on	WO 9935262
JP 2002500043	W	Based on	WO 9935262

PRIORITY APPLN. INFO: US 1998-27287 19980220; US 1998-3886 19980107; US 1998-75409P 19980220

AN 1999-430394 [36] WPIDS

CR 1997-480153 [44]; 1999-590729 [50]; 2002-556723 [59]; 2002-626537 [67]

AB WO 9935262 A UPAB: 20021022

NOVELTY - Isolated apoptosis inducing molecule II (AIM II) polypeptides and nucleic acids, are new.

DETAILED DESCRIPTION - (A) A novel isolated polypeptide comprises a member selected from:

(a) an apoptosis inducing molecule (II) (AIM II) N-terminal deletion mutant which has the amino acid sequence shown in sequence (II) (240 amino acids in length), provided that the amino acid sequence has a deletion of at least the first N-terminal amino acid residue but not more than the first 114 N-terminal amino acid residues of sequence (II);

(b) a polypeptide having an amino acid sequence at least 95% identical to an amino acid sequence identical to (a); and

(c) a polypeptide having an amino acid sequence identical to that of (a) except for at least one amino acid substitution.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (PN) 1169 bp (sequence given in the specification), encoding a polypeptide as in (A);

(2) a vector, and its method of production;

(3) a recombinant host cell and its method of production comprising introducing a recombinant vector as in (3) into a host cell;

(4) an isolated nucleic acid molecule (NAM) comprising a nucleotide sequence (NS) at least 95% identical to a sequence selected from:

(a) a NS encoding amino acids from 1 to 240 or 2 to 240 of sequence (II);

(b) a NS encoding an amino acid sequence encoded by a cDNA clone contained in ATCC No. 97689 or 97483;

(c) a NS encoding an AIM II polypeptide transmembrane domain, polypeptide intracellular domain or polypeptide having extracellular and intracellular domains but lacking the transmembrane domain; and

(d) a NS complementary to any of the NSs above;

(5) an isolated NAM comprising a PN which encodes an amino acid sequence of an epitope-bearing portion of an AIM II polypeptide as in sequence (II);

(6) (8) an isolated NAM selected from:

(a) at least 20 contiguous nucleotides of sequence (I) (1169 nucleotides in length), provided that the isolated NAM is not sequence (XX) (503 nucleotides in length) or any subfragments;

(b) a NS complementary to a NS as in (a); and

(c) (c) a NAM at least 20 nucleotides in length that **hybridizes** under stringent **hybridization** conditions to a NAM having a NS shown in sequence (I);

(7) an isolated AIM II polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from:

(a) amino acids from 1 to 240 or 2 to 240 in sequence (II);

(b) an amino acid sequence encoded by a cDNA clone contained in ATCC 97689 or 97483;

(c) an amino acid sequence of an extracellular domain, transmembrane domain or intracellular domain of the AIM II polypeptide;

(d) an amino acid sequence of a soluble AIM II polypeptide having all or part of the extracellular and intracellular domain but lacking the transmembrane domain; and

(e) the amino acid sequence of an epitope-bearing portion of any one of the polypeptides above;

(8) an AIM II polypeptide selected from a polypeptide comprising amino acid residues from 13 to 20, 23 to 36, 69 to 79, 85 to 94, 167 to 178, 184 to 196 or 221 to 233 in sequence (II);

(9) a method for making a recombinant vector comprising inserting an isolated NAM as in (4) into a vector;

(10) a recombinant vector produced by a method as in (9);

(11) a method of making a recombinant host cell comprising introducing a recombinant vector as in (10) into a host cell; and

(12) a recombinant host cell produced by a method as in (11).

ACTIVITY - Antiallergic; antiinflammatory; immunomodulator; antidiabetic; antibacterial; immunosuppressive; neuroprotective; osteopathic; antirheumatic; antiarthritic; dermatological.

MECHANISM OF ACTION - The effects of AIM II transduction on tumor growth were evaluated in vivo. When MDA-MB-231 cells were inoculated into mammary fat pads, AIM II expression significantly inhibited tumor formation of MDA-MB-231 in nude mice, whereas the vector control MDA-MB-231/Neo cells showed no change in tumor growth as compared with that of the parental MDA-MB-231 cells. Similar tumor suppression in the MDA-MB-231/AIM II cells was also demonstrated in SCID mice. A histological examination of the tumors from AIM II expressing MDA-MB-231 cells or those from parental or vector control cells was performed. Parental or vector control MDA-MB-231 cells formed a large solid tumor mass filled with predominantly tumor cells with little or no cellular infiltrates.

In contrast, there was extensive necrosis observed even in small residual tumors formed by the MDA-MB-231/AIM II cells in nude

mice. Furthermore, in AIM II expressing tumors, there is a significant increase in number of infiltrating neutrophil cells. The average number of neutrophils per mm2 tumor size in wild type, Neo control, and AIM II transduced MDA-MB-231 tumors were 101 plus or minus 26, 77 plus or minus 16, and 226 plus or minus 38 respectively, based on the immunohistological staining using Gr-1 monoclonal antibody. The inhibitory effect of AIM II on tumor suppression was further validated in the syngeneic murine tumor model. Local expression of AIM II in MC-38 murine colon cancer cells resulted in complete suppression of tumor formation in 8 out of 10 C57BL/6 mice. Local production of AMI II also dramatically prolonged the survival of mice bearing MC-38 tumors.

USE - The AIM II polypeptides mediate apoptosis by stimulating clonal deletion of T-cells. They can be used to treat lymphoproliferative disease which results in lymphoadenopathy, to stimulate peripheral tolerance and cytotoxic T-cell mediated apoptosis. They can be used to stimulate peripheral tolerance, destroy some transformed cell lines, mediate cell activation and proliferation and are functionally linked as primary mediators of immune regulation and inflammatory response. They can be used to treat autoimmune disease e.g. systemic lupus erythematosis (SLE), immunoproliferative disease lymphadenopathy (IPL), angioimmunoproliferative lymphadenopathy (AIL), immunoblastive lymphadenopathy (IBL), diabetes, multiple sclerosis, allergies, graft versus host disease.

Antagonists to AIM II polypeptides may be used to treat cachexia which is a lipid clearing defect resulting from a systemic deficiency of lipoprotein lipase, which is believed to be suppressed by AIM II, to treat cerebral malaria in which AIM II may play a pathogenic role, to treat rheumatoid arthritis by inhibiting AIM II induced production of inflammatory cytokines, such as IL-1 in the synovial cells, to prevent graft-versus-host rejection by preventing the stimulation of the immune system in the presence of a graft, to inhibit bone resorption and therefore to treat and/or prevent osteoporosis. They can also be used as anti-inflammatory agents, to treat endotoxic shock, and prevent activation of the HIV virus. The products can also be used for detection, diagnosis and prognosis. They can be used in mammals e.g. monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans.

Dwg.0/2

L12 ANSWER 24 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-061918 [05] WPIDS
CROSS REFERENCE: 2000-271403 [23]; 2000-647065 [53]
DOC. NO. CPI: C2000-017064
TITLE: New human interleukin-17 receptor like protein, e.g. to **treat** disorders relating to cellular activation.
DERWENT CLASS: B04 D16
INVENTOR(S): RUBEN, S M; SHI, Y
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9914240	A1	19990325	(200005)*	EN	132

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC

MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT UA UG US UZ VN YU ZW
AU 9894824 A 19990405 (200005)
EP 1015488 A1 20000705 (200035) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9914240	A1	WO 1998-US19121	19980916
AU 9894824	A	AU 1998-94824	19980916
EP 1015488	A1	EP 1998-948201	19980916
		WO 1998-US19121	19980916

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9894824	A	Based on	WO 9914240
EP 1015488	A1	Based on	WO 9914240

PRIORITY APPLN. INFO: US 1997-59133P 19970917
AN 2000-061918 [05] WPIDS
CR 2000-271403 [23]; 2000-647065 [53]
AB WO 9914240 A UPAB: 20001205
NOVELTY - Nucleic acid molecules (NAM's) encode human interleukin (IL)-17 receptor like protein (IL17RLP) (P1) and are obtained from a cDNA library of human adult pulmonary tissue.
DETAILED DESCRIPTION - (A) NAM has a polynucleotide (PN) having nucleotide (nt) sequence (NS) at least 95% identical to:
(a) NS encoding P1 having complete amino acid (aa) sequence (CAS) (I) (aa -19 to 407) of 426 aa (given in the specification);
(b) NS encoding P1 having CAS (I) except the N-terminal methionine (aa -18 to 407);
(c) NS encoding predicted mature P1 with a sequence at aa 1-407 in (I);
(d) NS encoding polypeptide (plp) comprising predicted extracellular domain (ED) of P1 having a sequence at aa 272-292 in (I);
(e) NS encoding soluble P1 with predicted ED and intracellular domains (ID), but lacking the predicted transmembrane domain (TD);
(f) NS encoding P1 having CAS encoded by cDNA clone (ATCC No. 209198);
(g) NS encoding P1 having CAS except N-terminal methionine encoded as in (f);
(h) NS encoding mature P1 having sequence encoded as in (f);
(i) NS encoding ED of P1 having sequence encoded as in (f), and
(j) NS complementary to NS' of (a)-(i).
INDEPENDENT CLAIMS are also included for the following:
(1) NAM comprising PN having NS at least 95% identical to:
(a) NS encoding plp with residues n-407 of (I), where n is an integer in the range of -19 to -5;
(b) NS encoding plp with residues -19-m of (I), where m is an integer in the range of 340-407;

(c) NS encoding plp having residues n-m of (I), where n and m are defined in (a) and (b);

(d) NS encoding plp having portion of CAS of IL17RLP encoded as in (Af), which excludes from 1-23 aa from the N-terminus of CAS encoded as in (Ag);

(e) NS encoding plp consisting of a portion of CAS of IL17RLP encoded as in (d), which excludes from 1-67 aa from the carboxy terminus of the CAS encoded as in (Ag), and

(f) NS encoding plp having a portion of CAS of IL17RLP encoded as in (d), which includes a combination of any of the N- and carboxy terminal deletions in (d) and (e);

(2) NAM comprising PN **hybridizing** to PN having NS identical (Aa)-(Aj), where the PN which **hybridizes** does not **hybridize** to PN having a NS with only A or T residues;

(3) NAM comprising PN encoding a sequence of an epitope-bearing portion of P1 having a sequence as in (Aa)-(Ai);

(4) making recombinant vector (RV) by inserting NAM of (A) into RV;

(5) RV produced by (4);

(6) making a recombinant host cell (RHC) by introducing RV of (5) into it;

(7) RHC produced by (6);

(8) P1 comprising an aa sequence at least 95% identical to:

(a) sequence of a full-length P1 having CAS (I) (aa -19 to 407);

(b) sequence of a full-length P1 having CAS (I) except the N-terminal methionine (aa -18 to 407);

(c) sequence of a mature P1 having CAS (I) (aa 1 to 407);

(d) sequence of predicted ED of P1 having a complete (I) (aa 1 to 271);

(e) sequence of a soluble P1 having predicted ED and ID, but lacking the predicted TD;

(f) CAS encoded as in (Ag);

(g) CAS except the N-terminal methionine encoded as in (Ag);

(h) CAS of a mature IL17RLP encoded as in (Af), and

(i) CAS of ED of an IL17RLP encoded as in (Ag);

(9) plp comprising an epitope-bearing portion of P1 which is selected from plp having aa's Ser-14 to Val-22, Cys-24 to Pro-32, Ile-41 to Arg-49, Thr-89 to Val-97, Thr-110 to Lys-118, Ala-144 to Ser-152, Thr-240 to Val-248, Gly-258 to Thr-267, Leu-280 to Gly-288, Cys-4004 to Glu-412, Pro-425 to Ser-423, Gly-409 to Glu-417, and Cys-404 to Leu-426 in (I);

(10) an antibody (Ab) specific for P1 of (8), and

(11) NAM comprising PN having a sequence at least 95% identical to NS of:

(a) (II) of 409 nt;

(b) (III) of 327 nt;

(c) a portion of (IV) of 1816 nt where the portion comprises at least 50 contiguous nt from nt 50-650;

(d) a portion of (IV) having nt's 50-1800, 100-1800, 200-1800, 400-1800, 500-1800, 600-1800, 50-650, 100-650, 200-650, 300-650, 400-650, 500-650, 50-500, 100-500, 200-500, 200-500, 300-500, 400-500, 50-400, 100-400, 200-400, 300-400, 50-300, 100-300, 200-300, 50-200, 100-200, and 50-100; and

(e) complementary to NSs in (a)-(d) (all sequences are given in the specification).

ACTIVITY - The IL17RLP activates signal transduction pathways resulting in stimulation of NF-kappaB transcription factor family,

secretion of IL-6 and costimulation of T-cell proliferation, induction of IL-6, IL-8, G-CSF, prostaglandin E (PGE2) and intracellular adhesion molecule (ICAM-1) expression, regulation of hematopoietic stem and progenitor cell growth and expansion, myelosuppressive activity for stem and immature subsets of myeloid progenitors, activation and stimulation of hematopoiesis (neutrophil hematopoiesis), enhancement of erythropoiesis, suppression of lymphopoiesis and myelopoiesis and strong suppression of monocytopoiesis, antigenicity (ability to bind (or compete with P1 for binding) to anti-IL17RLP Ab), immunogenicity (ability to generate Ab to P1), the ability to form polymers with other P1 or P1-like polypeptides, and ability to bind to a receptor or ligand for P1.

USE - P1's and agonists can be used to treat disorders relating to cellular activation, hemostasis, angiogenesis, tumor metastasis, cellular migration and ovulation, and neurogenesis. They can also be used to enhance host defenses against resistant chronic and acute infections, e.g. mycobacterial infections via the attraction and activation of microbial leukocytes. IL17RLP may also be used to increase T-cell proliferation by the stimulation of IL-2 biosynthesis for the treatment of T-cell mediated autoimmune diseases and lymphocytic leukemias, to regulate hematopoiesis by regulating the activation and differentiation of various hematopoietic progenitor cells, e.g. to release mature leukocytes from the bone marrow following chenotherapy, i.e. in stem cell mobilization or to treat sepsis. The products can also be used for the diagnosis or treatment of immune system related disorders e.g. tumors, cancers, interstitial lung disease (such as Langehans cell granulomatosis), and any disregulation of immune cell function including autoimmunity, arthritis, leukemias, lymphomas, immunosuppression, immunity, humoral immunity, inflammatory bowel disease, or myelo suppression. Antagonists may be used to inhibit the activation of macrophages and their precursors, and of neutrophils, basophils, B lymphocytes and some T-cell subsets, e.g. activated and CD8 cytotoxic T cells and natural killer cells, in certain auto-immune and chronic inflammatory and infective diseases, e.g. autoimmune diseases including multiple sclerosis and insulin-dependent diabetes, infectious diseases including silicosis, sarcoidosis, idiopathic pulmonary fibrosis by preventing the activation of mononuclear phagocytes, idiopathic hypereosinophilic syndrome by preventing eosinophil production, or rheumatoid arthritis by preventing the activation of monocytes in the synovial fluid in the joints of patients or to treat or prevent inflammation. Dwg.0/3

L12 ANSWER 25 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97183606 EMBASE
DOCUMENT NUMBER: 1997183606
TITLE: Regression of papillomas induced by cottontail rabbit papillomavirus is associated with infiltration of CD8+ cells and persistence of viral DNA after regression.
AUTHOR: Selvakumar R.; Schmitt A.; Iftner T.; Ahmed R.; Wettstein F.O.
CORPORATE SOURCE: F.O. Wettstein, Dept. of Microbiology/Immunology, UCLA School of Medicine, 10833 Le Conte Ave., Los Angeles, CA 90095-1747, United States
SOURCE: Journal of Virology, (1997) 71/7 (5540-5548).

Refs: 51
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cottontail rabbit papillomavirus (CRPV) is a highly oncogenic papillomavirus and has been successfully used as a model to develop protective vaccines against papillomaviruses. Papillomas induced by the virus may spontaneously regress, suggesting that CRPV can also serve as a model to develop **therapeutic** vaccines. As a first step toward this goal, we have analyzed immunologic and viral aspects associated with papilloma regression and have identified several features unique to regression. Immunohistochemical staining of biopsies from growing and regressing papillomas and from sites after complete regression showed infiltration of CD8+ cells into the basal and suprabasal layers of the epidermis only during active regression. In situ **hybridizations** with mRNA-specific probes were strongly positive for E6 and E7 mRNAs during regression, but no late mRNA was present. Viral DNA was **detected** by in situ **hybridization** during regression but not after regression. However, analysis by PCR revealed persistence of viral DNA for several months at the majority of regression sites. The results suggest that stimulation of a strong CD8+ response to virus-infected cells is important for an effective **therapeutic** vaccine and that special attention should be given to the suppression of latent **infection**.

L12 ANSWER 26 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 97:760656 SCISEARCH
THE GENUINE ARTICLE: XZ994
TITLE: Depletion of CD8(+) T lymphocytes by murine monoclonal CD8 antibodies and restored specific T cell proliferation in vivo in a patient with chronic hepatitis C
AUTHOR: Kiefersauer S; Reiter C; Eisenburg J; Diepolder H M; Rieber E P; Riethmuller G; Gruber R (Reprint)
CORPORATE SOURCE: UNIV MUNICH, INST IMMUNOL, GOETHESTR 31, D-80336 MUNICH, GERMANY (Reprint); UNIV MUNICH, INST IMMUNOL, D-80336 MUNICH, GERMANY; UNIV MUNICH, KLINIKUM GROSSHADERN, DEPT MED 2, D-8000 MUNICH, GERMANY; KRANKENHAUS BARMHERZIGEN BRUDER, MUNICH, GERMANY; CARL GUSTAV CARUS UNIV DRESDEN, INST IMMUNOL, DRESDEN, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: JOURNAL OF IMMUNOLOGY, (15 OCT 1997) Vol. 159, No. 8, pp. 4064-4071.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cellular immune mechanisms, especially those mediated by CD8(+) T cells, are important in the pathogenesis and control of viral **infections**. On the other hand, as shown for chronic lymphocytic choriomeningitis virus **infection** in the mouse, CD8(+) T cells may not only hinder the elimination of a virus, but make the host unresponsive to a second viral **infection**, In hepatitis C virus (HCV) **infections**, at least 50% of the patients become chronically infected, despite the **detection** of HCV-specific **CTL** and a specific proliferative response to HCV Ags in PBL and in lymphocytes isolated from the liver, To better understand the immunopathologic mechanisms of CD8(+) cells in vivo and to search for a potential **treatment**, we applied murine CD8 mAbs to a patient with **therapy**-resistant chronic HCV. A drastic reduction of CD8(+) circulating lymphocytes, a reduction of CD8 molecule density, and complement fixation on CD8(+) cells were observed, The reduction of CD8(+) cells was compensated partially by an elevation of CD4(+) cells. High concentrations of neutralizing human anti-mouse Abs were induced, After the Ab infusions, the CD4/CD8 ratio In peripheral blood increased from 1.6 to values of about 3 during **therapy**, and gradually decreased to 2.3 1 yr after the last mAb infusion. A continuing decrease of serum aminotransferases and clinical improvement was observed, Interestingly, after initiation of **treatment**, a significant proliferative response to HCV-specific Ags became measurable.

L12 ANSWER 27 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97083738 EMBASE
DOCUMENT NUMBER: 1997083738
TITLE: Humoral, mucosal, and cellular immunity in response to a **human** immunodeficiency **virus** type 1 **immunogen** expressed by a Venezuelan equine encephalitis virus vaccine vector.
AUTHOR: Caley I.J.; Betts M.R.; Irlbeck D.M.; Davis N.L.; Swanstrom R.; Frelinger J.A.; Johnston R.E.
CORPORATE SOURCE: R.E. Johnston, Dept. of Microbiology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, NC 27599, United States
SOURCE: Journal of Virology, (1997) 71/4 (3031-3038).
Refs: 54
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A molecularly cloned attenuated strain of Venezuelan equine encephalitis virus (VEE) has been genetically configured as a replication-competent vaccine vector for the expression of heterologous viral proteins (N. L. Davis, K. W. Brown, and R. E. Johnston, J. Virol. 70:3781-3787, 1996). The matrix/capsid (MA/CA) coding domain of **human** immunodeficiency **virus** type 1 (**HIV**-1) was cloned into the VEE vector to **determine** the ability of a VEE vector to stimulate an anti-**HIV** immune response in mice. The VEE-MA/CA vector replicated rapidly in the cytoplasm of baby hamster kidney (BHK) cells and expressed large quantities of antigenically identifiable MA/CA protein. When injected subcutaneously into BALB/c mice, the vector

invaded and replicated in the draining lymphoid tissues, expressing **HIV**-1 MA/CA at a site of potent immune activity. Anti-MA/CA immunoglobulin G (IgG) and IgA antibodies were present in serum of all immunized mice, and titers increased after a second booster inoculation. IgA antibodies specific for MA/CA were **detected** in vaginal washes of mice that received two subcutaneous immunizations. **Cytotoxic T-lymphocyte** responses specific for MA/CA were **detected** following immunization with the MA/CA-expressing VEE vector. These findings demonstrate the ability of a VEE-based vaccine vector system to stimulate a comprehensive humoral and cellular immune response. The multifaceted nature of this response makes VEE an attractive vaccine for immunization against virus **infections** such as **HIV**-1, for which the correlates of protective immunity remain unclear, but may include multiple components of the immune system.

L12 ANSWER 28 OF 37 MEDLINE
ACCESSION NUMBER: 97413372 MEDLINE
DOCUMENT NUMBER: 97413372 PubMed ID: 9269787
TITLE: Immunohistochemical **detection** of the Epstein-Barr virus-encoded latent membrane protein 2A in Hodgkin's disease and **infectious** mononucleosis.
AUTHOR: Niedobitek G; Kremmer E; Herbst H; Whitehead L; Dawson C W; Niedobitek E; von Ostau C; Rooney N; Grasser F A; Young L S
CORPORATE SOURCE: Institute for Cancer Studies and the Department of Pathology, University of Birmingham, UK.
SOURCE: BLOOD, (1997 Aug 15) 90 (4) 1664-72. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 19980206
Entered Medline: 19970924

AB We describe two new monoclonal antibodies specific for the Epstein-Barr virus (EBV)-encoded latent membrane protein 2A (LMP2A) that are suitable for the immunohistochemical analysis of routinely processed paraffin sections. These antibodies were applied to the immunohistochemical **detection** of LMP2A in Hodgkin's disease (HD). LMP2A-specific membrane staining was seen in the Hodgkin and Reed-Sternberg (HRS) cells of 22 of 42 (52%) EBV-positive HD cases, but not in 39 EBV-negative HD cases. In lymphoid tissues from patients with acute **infectious** mononucleosis (IM), interfollicular immunoblasts were shown to express LMP2A. This is the first demonstration of LMP2A protein expression at the single-cell level in EBV-associated lymphoproliferations in vivo. The **detection** of LMP2A protein expression in HD and IM is of importance in view of the proposed role of this protein for maintaining latent EBV **infection** and its possible contribution for EBV-associated transformation. Because LMP2A provides target epitopes for EBV-specific **cytotoxic T cells**, the expression of this protein in HRS cells has implications for the

immunotherapeutic approaches to the **treatment** of HD.

L12 ANSWER 29 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:563096 BIOSIS
DOCUMENT NUMBER: PREV199799292452
TITLE: Nasal NK- and T-cell lymphomas share the same type of Epstein-Barr virus latency as nasopharyngeal carcinoma and Hodgkin's disease.
AUTHOR(S): Chiang, Alan K. S.; Tao, Qian; Srivastava, Gopesh (1); Ho, Faith C. S.
CORPORATE SOURCE: (1) Dep. Pathol., Univ. Pathol. Build., Queen Mary Hosp. Compound, Pokfulam Rd., Hong Kong Hong Kong
SOURCE: International Journal of Cancer, (1996) Vol. 68, No. 3, pp. 285-290.
ISSN: 0020-7136.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Nasal T/NK-cell lymphomas can be further separated into those of natural killer (NK) cell lineage or of T-cell lineage, with differences in cellular phenotype, T-cell receptor (TcR) gene rearrangement and TcR transcript expression. Both NK- and T-cell subtypes are closely associated with Epstein-Barr virus (EBV). In this study, EBV gene expression was **determined** in 23 cases of nasal lymphoma (NL) by in situ **hybridisation** (ISH), reverse transcriptase-polymerase chain reaction (RT-PCR) and immunohistochemistry (IH). Of the 23 cases, 19 were classified as NK-cell and 4 as T-cell tumours. ISH for EBV-encoded small non-polyadenylated RNAs showed that all cases, whether NK or T, harboured EBV in virtually all tumour cells. RT-PCR demonstrated that NL of both subtypes expressed EBNAI of the QUK splice pattern, the latent membrane proteins, LM PI and 2 and the BamHI A rightward transcripts in the absence of EBNA2 mRNAs, compatible with the latency type 11 pattern. In addition, analysis of EBV protein expression by IH revealed a heterogeneous pattern of EBV gene expression at the single-cell level consisting of both LMPI+ and LMPI- tumour cells, suggesting a mixture of latency I and II. Although 2 early lytic transcripts, BZLFI and BHRFI, were also **detected** in 13 and 10 cases, respectively, the lack of ZEBRA staining in any case indicates that these lytic transcripts are most likely expressed by rare cells in the biopsies entering lytic cycle. The viral transcriptional pattern similar to that of nasopharyngeal carcinoma and Hodgkin's disease suggests that EBV can exploit common regulatory mechanisms for gene transcription in diverse host cell types. Down-regulation of **immunogenic** proteins (EBNA2-EBNA6) in nasal lymphoma may enable tumour cells to evade host **cytotoxic T-cell** surveillance.

L12 ANSWER 30 OF 37 MEDLINE
ACCESSION NUMBER: 96071442 MEDLINE
DOCUMENT NUMBER: 96071442 PubMed ID: 7585062
TITLE: Transfer of **HIV**-1-specific **cytotoxic T lymphocytes** to an **AIDS** patient leads to selection for mutant **HIV** variants and subsequent disease progression.
COMMENT: Comment in: Nat Med. 1995 Apr;1(4):304-5
AUTHOR: Koenig S; Conley A J; Brewah Y A; Jones G M; Leath S; Boots L J; Davey V; Pantaleo G; Demarest J F; Carter

C; +
CORPORATE SOURCE: MedImmune, Inc., Gaithersburg, Maryland 20878, USA.
SOURCE: NATURE MEDICINE, (1995 Apr) 1 (4) 330-6.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951228

AB An **HIV**-1-seropositive volunteer was infused with an expanded autologous **cytotoxic T lymphocyte** (**CTL**) clone directed against the **HIV**-1 nef protein. This clone was adoptively transferred to **determine** whether supplementing **CTL** activity could reduce viral load or improve clinical course. Unexpectedly, infusion was followed by a decline in circulating CD4+ T cells and a rise in viral load. Some of the **HIV** isolates obtained from the plasma or CD4+ cells of the patient were lacking the nef epitope. These results suggest that active **CTL** selection of viral variants could contribute to the pathogenesis of **AIDS** and that clinical progression can occur despite high levels of circulating **HIV**-1-specific **CTLs**.

L12 ANSWER 31 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1995-082473 [11] WPIDS
DOC. NO. CPI: C1995-037038
TITLE: New purified interleukin-15 - which induces T cell proliferation and differentiation, used for the **treatment** of tumours and viral **infection**.
DERWENT CLASS: B04 D16
INVENTOR(S): ANDERSON, D M; EISENMAN, J R; FUNG, V; GRABSTEIN, K H; RAUCH, C
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
ZA 9402636	A	19941228	(199511)*	EN	47

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
ZA 9402636	A	ZA 1994-2636	19940418

PRIORITY APPLN. INFO: ZA 1994-2636 19940418
AN 1995-082473 [11] WPIDS
AB ZA 9402636 A UPAB: 19950322
(A) An isolated DNA sequence encoding a polypeptide exhibiting mammalian interleukin-15 (IL-15) activity is claimed, where the DNA sequence is selected from: (a) a DNA sequence encoding a mammalian IL-15 polypeptide comprising the sequence: Asn Trp Val Asn Val Ile

Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln Val Ile Ser Xaa1 Glu Ser Gly Asp Xaa2 Xaa3 Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Xaa4 Leu Ser Ser Asn Gly Asn Xaa5 Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn Thr Ser Xaa1 = Leu or His; Xaa2 = Ala or Thr; Xaa3 = Ser or Asp; Xaa4 = Ser or Ile; Xaa5 = Val or Ile; and (b) DNA sequences that **detectably hybridise** to the DNA sequences of (a) or their complementary strands under conditions of high stringency and code on expression for a polypeptide with mammalian IL-15 biological activity. Also claimed are: (B) a recombinant expression vector comprising a DNA sequence encoding a polypeptide with mammalian IL-15 biological activity as in (A); (C) a host cell transformed or transfected with an expression vector as in (B); (D) an isolated biologically active IL-15 polypeptide compsn. comprising an amino acid sequence encoded by an isolated DNA sequence as in (A); and (E) an isolated DNA sequence encoding a precursor polypeptide of the biologically active IL-15 polypeptide, where the DNA has one of the two sequences (simian or human) given in the specification.

USE - The mature IL-15 is capable of signalling proliferation and/or differentiation of precursor or mature T cells and can be used to promote long-term in vitro culture of T-lymphocytes and T-cell lines. It can stimulate the activity of cytolytic T lymphocytes (**CTL**), lymphokine activated killer (LAK) cells and natural killer (NK) cells and expand the population of T cells that can destroy tumour cells and viral-infected cells. It can be used in patients with carcinomas, melanomas, sarcomas, leukaemia or lymphomas or patients infected with Herpesviridae including cytomegalovirus, Polyomaviridae, Retroviridae, including **HIV**, influenza virus, Hepadnaviridae, hepatitis A, B, C or D or hepatitis delta. It can also be used to suppress a form of anaemia.

L12 ANSWER 32 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:37352 BIOSIS
DOCUMENT NUMBER: PREV199598051652
TITLE: Induction by concanavalin A of specific mRNAs and cytolytic function in a CD8-positive T cell hybridoma.
AUTHOR(S): Gu, Jing Jin; Harriss, June V.; Ozato, Keiko; Gottlieb, Paul D. (1)
CORPORATE SOURCE: (1) Dep. Microbiol., Univ. Tex., Austin, TX 78712 USA
SOURCE: Journal of Immunology, (1994) Vol. 153, No. 10, pp. 4408-4417.
ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English

AB A previous report from this laboratory described the production of CD8+, class I-specific T cell hybridomas which developed specific cytolytic activity and the ability to secrete IL-2 upon Con A or specific Ag stimulation. Unlike normal lymphocytes or long-term **CTL** lines for which exposure to Ag triggers both differentiation and proliferation, T cell hybridoma lines can be activated functionally against a background of continuous proliferation. They therefore provide a unique system with which to study the molecular events involved in the induction of cytolytic function. The expression of mRNA from a series of genes was

evaluated by Northern **hybridization** at various times after Con A stimulation of the H-2L-d-specific CD8+ 3D9 hybridoma. Induction of the c-fos proto-oncogene by 45 min poststimulation was followed shortly by c-myc induction. Perforin mRNA was expressed at a low level in the unstimulated hybridomas, but was down-regulated upon Con A stimulation to levels undetectable by PCR. Interestingly, production of granzyme A mRNA was strongly induced by 45 min after Con A stimulation. In the CD8+ RT-1.3G3 hybridoma, which is nonlytic and specific for the **HIV**-1 envelope glycoprotein, c-fos but not granzyme A mRNA was induced by 45 min poststimulation, and no granzyme A mRNA was **detectable** at any time. Thus, a significant role for granzyme A in the induction of cytolytic activity is suggested. Cytolysis by the 3D9 hybridoma involved both target cell membrane damage and DNA fragmentation, and both Ca-2+-dependent and Ca-2+-independent cytolysis were observed. Although TNF-alpha mRNA was induced by 4 h poststimulation, Ab to TNF-alpha failed to inhibit the Ca-2+-independent lysis observed, leaving the basis for the observed Ca-2+-independent lysis unexplained.

L12 ANSWER 33 OF 37 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 94330495 MEDLINE
DOCUMENT NUMBER: 94330495 PubMed ID: 8053485
TITLE: **Detection** and characterization of Epstein-Barr virus in clinical specimens.
AUTHOR: Ambinder R F; Mann R B
CORPORATE SOURCE: Department of Oncology, Johns Hopkins School of Medicine, Baltimore, Maryland.
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1994 Aug) 145 (2) 239-52. Ref: 110
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940914
Last Updated on STN: 19940914
Entered Medline: 19940908

AB Epstein-Barr virus (EBV) is associated with a wide spectrum of benign and malignant diseases. Recent additions to the list include oral hairy leukoplakia; a subset of Hodgkin's lymphomas, particularly those with mixed cellularity histology or those occurring in underdeveloped countries; a subset of diffuse large cell/immunoblastic lymphoma in the immunocompromised, particularly primary central nervous system lymphoma; a subset of peripheral T cell lymphomas; and a subset of gastric carcinomas, particularly undifferentiated carcinomas. There are several distinctive aspects of the biology of the virus that are important in investigations of virus in clinical specimens. The presence of repeated elements in the genome facilitates **detection** of viral nucleic acids by a variety of **hybridization** techniques as well as the characterization of the clonality of virus-infected tissues. Latent viral **infection** is associated with several different patterns of viral gene expression in infected cells. Latent gene products are important because of their growth-regulating and

-transforming properties as well as the potent **cytotoxic T cell** response they elicit. The abundant expression of the EBER RNA transcripts makes possible the sensitive **detection** of latent **infection** in EBV-associated tumors. Lytic **infection** can be inhibited by antiviral nucleoside analogues. Two lytic gene products are of special interest because of their homology to the cellular proteins BCL-2 and interleukin-10. Two viral biotypes or strains with different properties in terms of lymphocyte immortalization and transformation have recently been characterized. Current evidence suggests a differential biotype association with particular malignancies. Characterization of the association of EBV with various disease processes promises to be important for diagnosis and **treatment** as well as for a better understanding of the epidemiology and pathogenesis of these diabetes.

L12 ANSWER 34 OF 37 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 91170737 MEDLINE
DOCUMENT NUMBER: 91170737 PubMed ID: 1672337
TITLE: The role of CD4+ cells in sustaining lymphocyte proliferation during lymphocytic choriomeningitis virus **infection**.
AUTHOR: Kasaian M T; Leite-Morris K A; Biron C A
CORPORATE SOURCE: Division of Biology and Medicine, Brown University, Providence, RI 02912.
CONTRACT NUMBER: CA-41268 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1991 Mar 15) 146 (6) 1955-63. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19910512
Last Updated on STN: 19950206
Entered Medline: 19910422

AB The murine immune response to lymphocytic choriomeningitis virus (LCMV) **infection** involves the activation of CD8+, class I MHC-restricted and virus-specific **CTL**. At times coinciding with **CTL** activation, high levels of IL-2 gene expression and production occur, the IL-2R is expressed, and T cell blastogenesis and proliferation are induced. We have previously found that, although both CD4+ and CD8+ T cell subsets transcribe IL-2, the CD4+ subset appears to be the major producer of IL-2 whereas the CD8+ subset appears to be the major proliferating population when the subsets are separated after activation in vivo. The studies presented here were undertaken to examine the contribution made by the CD4+ subset to lymphocyte proliferation in vivo. Responses to LCMV **infection** were examined in intact mice and in mice depleted of CD4+ or CD8+ subsets by antibody **treatments** in vivo. Protocols were such that in vivo **treatments** with anti-CD4 or anti-CD8 depleted the respective subset by greater than 90%. In situ **hybridizations** demonstrated that the IL-2 gene was expressed in non-B lymphocytes isolated from either CD4+ cell-depleted or CD8+ cell-depleted mice on day 7 post-**infection** with LCMV. When placed in culture, however, cells from CD8+ cell-depleted mice produced significantly higher levels of **detectable** IL-2 than did cells isolated

from CD4+ cell-depleted mice on day 7 post-**infection**. IL-2 was apparently produced in vivo in mice depleted of either CD4+ or CD8+ cells, as expression of the gene for the p55 chain of the IL-2R, IL-2 responsiveness, and lymphocyte proliferation were observed with cells isolated from both sets of mice. Lymphocyte proliferation was shown to be sustained in mice depleted of CD4+ cells in vivo by three criteria: 1) non-B lymphocytes isolated from infected mice depleted of CD4+ cells underwent more DNA synthesis than did those isolated from uninfected mice or from infected mice depleted of CD8+ cells; 2) leukocyte yields were expanded during **infection** of CD4+ cell-depleted mice; and 3) CD8+ cell numbers were increased during **infection** of CD4+ cell-depleted mice. The majority of non-B lymphocytes having the characteristics of blast lymphocytes was recovered in the CD8+ populations isolated from infected CD4+ cell-depleted mice. These findings suggest that the requirement for the CD4+ subset to sustain CD8+ lymphocyte proliferation in vivo is limited, and that CD4+ and CD8+ cell types can function independently in many aspects of their responses to viral **infections**.

L12 ANSWER 35 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:410321 BIOSIS
DOCUMENT NUMBER: BA92:77286
TITLE: SERUM HBV DNA **DETECTED** BY PCR IN DOT BLOT NEGATIVE HBV CHRONIC CARRIERS WITH ACTIVE LIVER DISEASE.
AUTHOR(S): MONJARDINO J; VELOSA J; THOMAS H C; DE MOURA M C
CORPORATE SOURCE: DEP. MED., ST. MARY'S HOSP., LONDON W2, UK.
SOURCE: J HEPATOL (AMST), (1991) 13 (1), 44-48.
CODEN: JOHEEC. ISSN: 0168-8278.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB A group of forty-nine HBV chronic carriers with histologically confirmed active liver disease and undetected serum HBV DNA by blot-**hybridisation** were re-investigated using the polymerase chain reaction (PCR) for amplification of serum DNA. The group comprised 16 persistently serum HBeAg-negative and thirty-three anti-HBe-positive patients. The use of PCR followed by Southern blot analysis has increased the sensitivity of HBV DNA **detection** by about 10-50 virions per ml of serum. Our results showed 14/16 (87.5%) of the HBeAg-positive group and 27/33 (81.8%) of the anti-HBe group to be positive for HBV DNA using PCR. Of the nine cases where HBV DNA was undetected four were positive for markers of hepatitis delta virus (HDV) **infection**. Demonstration of low level HBV replication associated with active liver disease in chronic HBV carriers where it was previously undetected meets a basic requirement for the proposed role of **cytotoxic T lymphocyte**-mediated immunopathogenesis in chronic hepatitis B and suggests a combined antiviral and immunotherapeutic approach to achieve eradication of the **infection**.

L12 ANSWER 36 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:111377 BIOSIS
DOCUMENT NUMBER: BA89:60868
TITLE: INTERLEUKIN 2-INDUCED PROLIFERATION OF MURINE NATURAL KILLER CELLS IN-VIVO.
AUTHOR(S): BIRON C A; YOUNG H A; KASAIAN M T

CORPORATE SOURCE: DIV. BIOL. AND MED., BOX G-B602, BROWN UNIV., PROVIDENCE, R.I. 02912.
SOURCE: J EXP MED, (1990) 171 (1), 173-188.
CODEN: JEMEAV. ISSN: 0022-1007.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB The growth factor, IL-2, was administered to mice to evaluate the in vivo responsiveness of NK cells to this factor. The immediate effects of this factor on NK cells were **determined** by examining cytotoxic activity at 18-24 h after a single **treatment** with rIL-2. Although moderate doses of rIL-2 (3 .times. 104 U) could be shown to activate existing cytotoxic cells on a per cell basis, higher doses (106 U) were required to elicit blast size killer cells. The elicited killer cells were characterized as NK cells by the following criteria: (a) they were readily induced in athymic mice; (b) they mediated killing of NK-sensitive YAC-1 target cells but not NK-resistant P815 target cells; and (c) they expressed the NK cell **determinants** asialo ganglio-n-tetraosylceramide and NK1.1, but not the T cell **determinants** CD3, L3T4, or Lyt-2. High-dose IL-2 **treatment** induced not only the appearance of blast size NK cells, but also the expansion of this population. After **treatments**, the number of large granular lymphocytes and the number of NK1.1+ cells were increased at least twofold. Analysis of DNA content within the NK1.1+ cell subset demonstrated that IL-2 preferentially drove NK1.1+ cells into S and G2/M phases of the cell cycle. The in vivo elicited blast lymphocytes were examined by Northern blot analysis and in situ **hybridization** for expression of the IL-2-R p55 .alpha. chain gene. As previous work from this laboratory has demonstrated that NK cells proliferate in response to IFNs and IFN inducers in vivo, blast lymphocytes were also prepared after IFN **treatments**. The NK cells were not induced to express **detectable** levels of the .alpha. chain gene under any of the conditions examined. Blast T lymphocytes, isolated at times during viral **infections** when IL-2 production can be demonstrated in vitro, were induced to transcribe the .alpha. chain gene. **Treatments** of euthymic mice with high-dose IL-2 also induced transcription of the .alpha.-chain gene in 41% of the non-B blast lymphocytes, but only background percentages of the NK1.1+ cells expressed the .alpha. chain gene. Transcription of the .alpha. chain gene was not induced in the NK cell-abundant athymic mice after IL-2 **treatment**. All of the in vivo elicited blast lymphocytes were induced to express IFN-.gamma.. Taken together, these data definitively demonstrate that IL-2 can induce NK cell proliferation and expansion in vivo. They also show that exposure to IL-2 in vivo, either by administration or endogenous production of the factor, induces transcription of the IL-2-R .alpha. chain gene in populations of cells containing T cell subsets. The results suggests, however, that murine NK cells are not induced to express high levels of the .alpha. chain gene in response to IL-2 in vivo.

L12 ANSWER 37 OF 37 MEDLINE
ACCESSION NUMBER: 86149322 MEDLINE
DOCUMENT NUMBER: 86149322 PubMed ID: 2869486
TITLE: Hybrid hybridoma producing a bispecific monoclonal antibody that can focus effector T-cell activity.
AUTHOR: Staerz U D; Bevan M J

CONTRACT NUMBER: AI19335 (NIAID)
CA25803 (NCI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1986 Mar) 83 (5) 1453-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
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Entered Medline: 19860410

AB Previous studies have shown that heteroconjugates of monoclonal antibodies in which one of the component antibodies is directed at the T-cell receptor and the other is directed against any chosen site can focus effector T cells to function at the targeted site. We report here the production of a hybrid hybridoma cell line, H1.10.1.6, which secretes large amounts of a bispecific hybrid antibody of the IgG2a class, that can focus T-cell activity. The parental hybridoma lines for the secondary fusion were F23.1, which secretes an antibody specific for an allotypic **determinant** on the T-cell receptor of most mouse strains, and 19E12, secreting an anti-Thy-1.1 antibody. The bispecific hybrid antibody was partially purified by hydroxylapatite chromatography and characterized by isoelectric focusing. It efficiently targets Thy-1.1-expressing tumor cells for lysis by F23.1 receptor-positive **cytotoxic T-cell** clones in vitro. Such hybrid antibodies produced by hybrid hybridoma cell lines may have application in the **therapeutic** targeting of tumors or sites of viral **infections** for attack by T cells.

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